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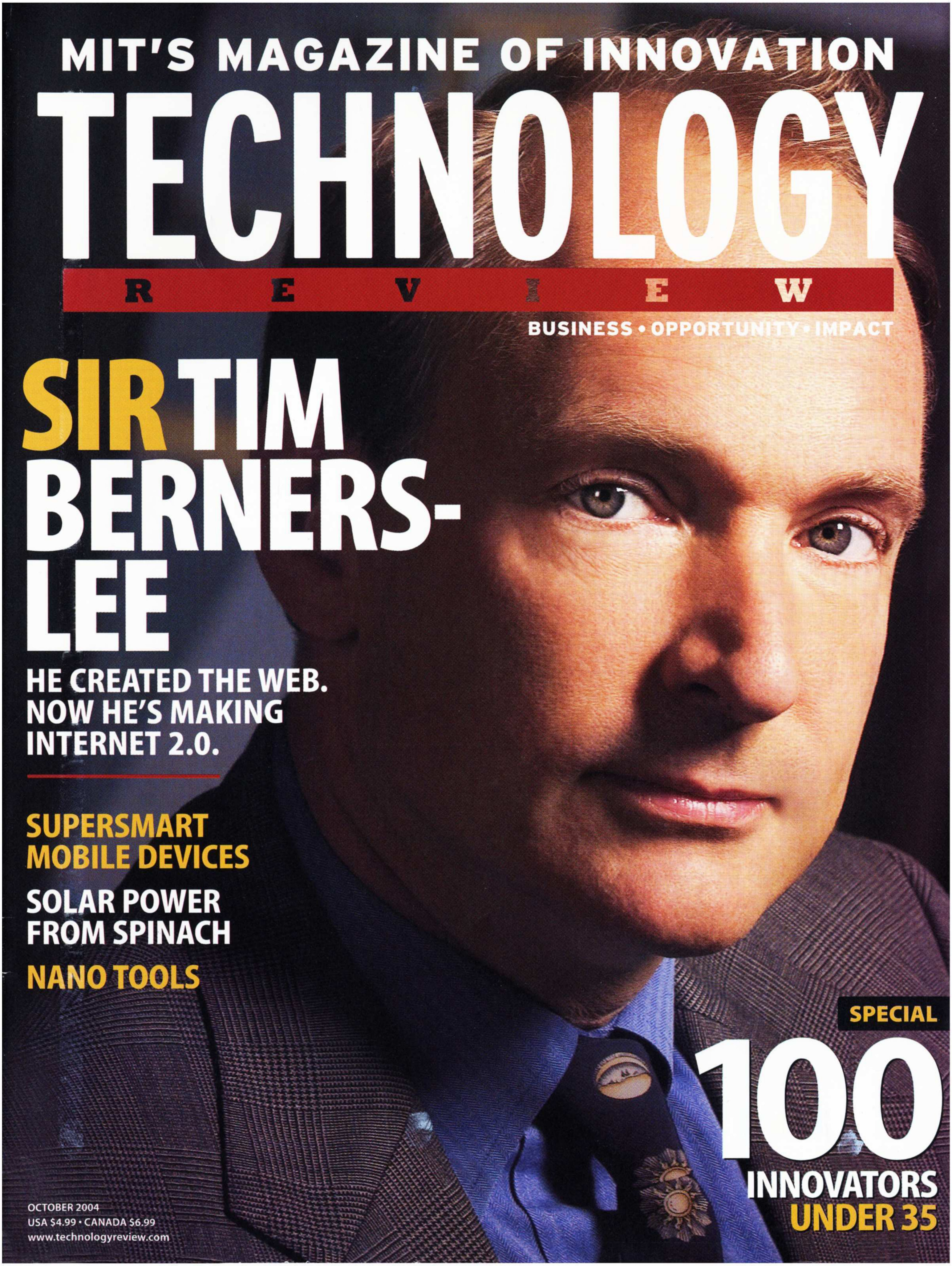

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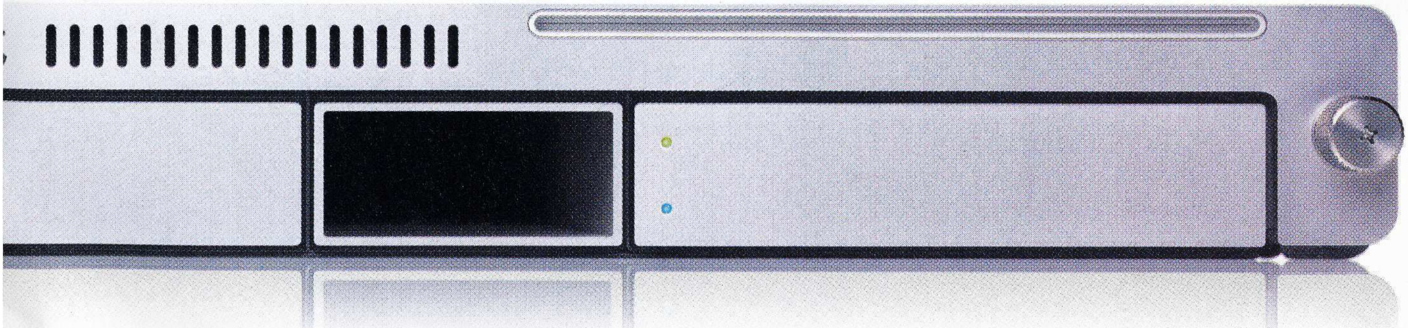

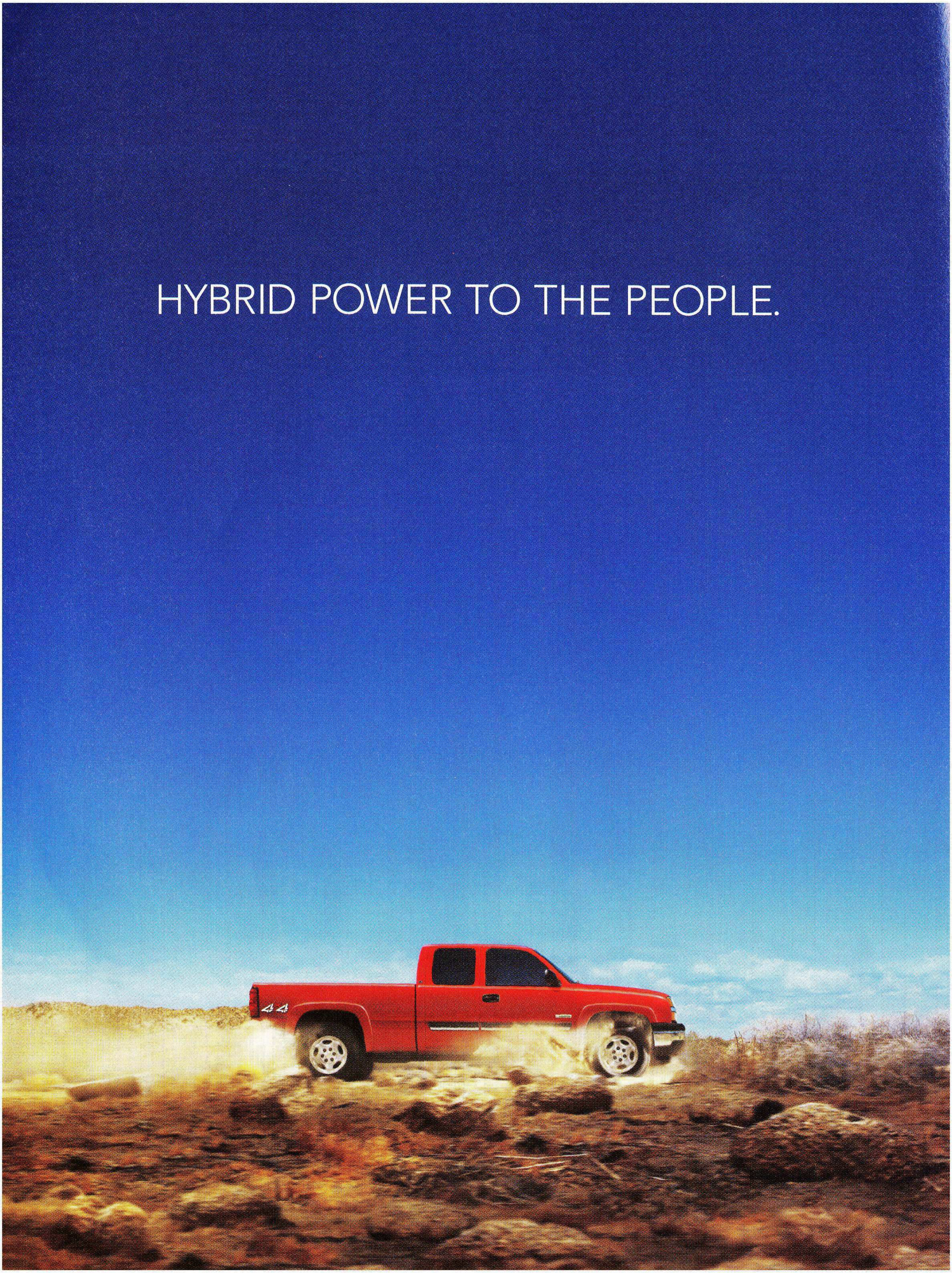
HYBRID POWER TO THE PEOPLE.

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Cover photographer: Bart Nagel; Grooming: Rae Bertellotti/Team

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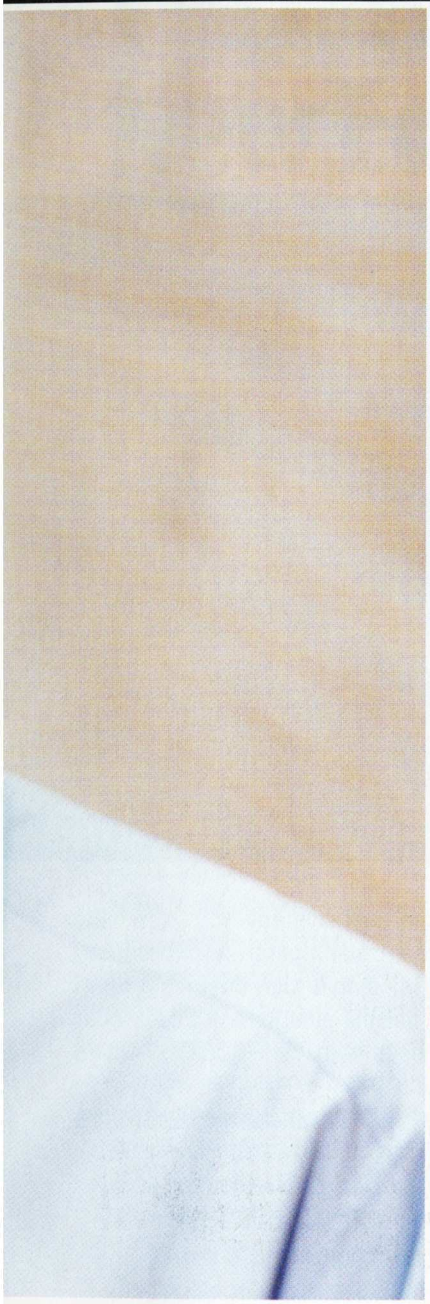
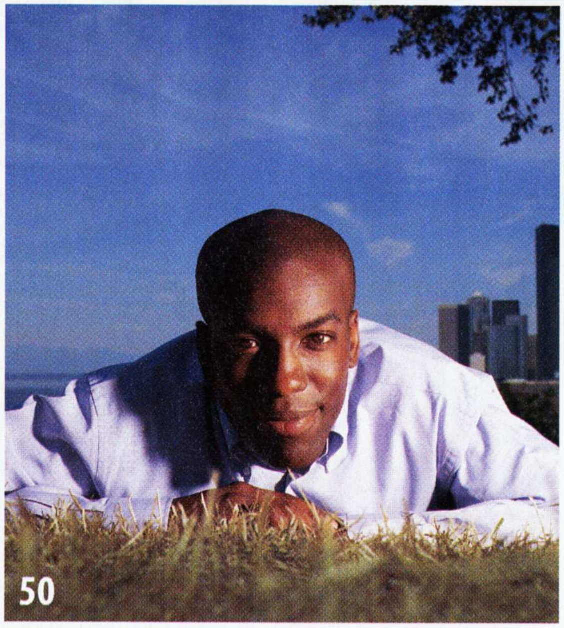
Technology Review
Volume 107, Number 8
October 2004

"Once you start with the basic Web idea, so much stuff becomes possible."—*Tim Berners-Lee, p. 45*





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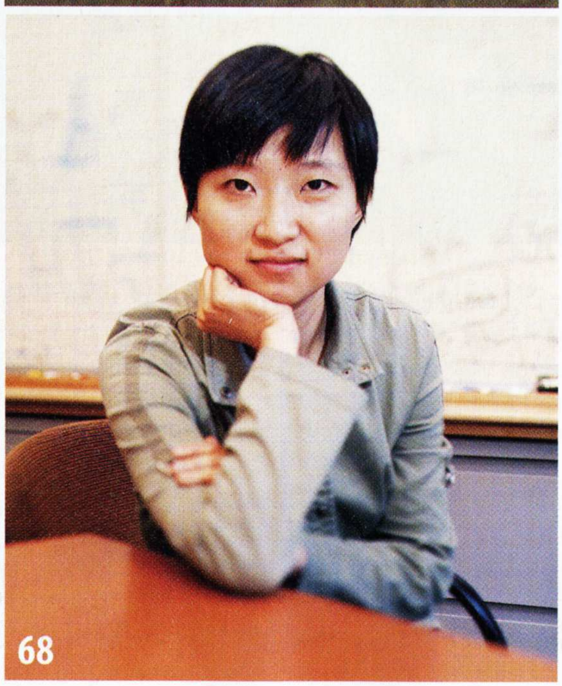

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IN EVERY ISSUE

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We Have a New Editor

THIS YEAR, *Technology Review* celebrates its 105th anniversary. And this year, also, we hire a new editor in chief.

For more than a century, the magazine has been led by gifted editors. For much of our history, the magazine was content to serve a small but influential audience of MIT graduates and leaders in business, research, government, and academia. It is only in recent years that *Technology Review* and its related businesses have begun to reach a larger audience of almost two million print and Web readers every month.

The strategy that initiated this growth was hatched in 1998, with an editorial blueprint developed and executed by John Benditt. John's editorial vision shaped much of what *Technology Review* is today—a magazine of innovation that focuses on the impact of emerging technologies. He pursued that vision in award-winning fashion and with great success. For the past two years, Bob Buderi has done the same, expanding our coverage to include a global marketplace and reach a global readership. Bob stepped down as editor in chief in June, in order to focus more on his writing, but he will continue to work at *Technology Review* as editor at large.

Succeeding John and Bob is a distinguished journalist: Jason Pontin. Jason was the editor of *Red Herring*, one of the most successful magazines of the '90s. As *Red Herring*'s editor, he once published an issue of 628 pages, weighing more than 1.5 kilograms. He was also the founding editor of an award-winning life sciences magazine, *Acumen Journal of Life Sciences*. He joins us to lead our efforts in print, online, and at events and conferences.

Jason grew up in Northern California but was educated in Great Britain, at Harrow School and the University of Oxford. He has written for many international newspapers and magazines, including the *Financial Times*, the *Economist*, *Wired*, and the *Believer*, and he is a frequent on-air guest of television and radio networks including ABC News, CNN, and National Public Radio.

Much has changed since the heady days of the '90s—and so must we. Under Jason's direction we will be presenting you with a fresh new design and format beginning with our January issue. The new *MIT Technology Review* will be authoritative yet engaging, credible and inviting, exciting and thoughtful, enlightening and challenging. It will be more accessible and provide more content than ever before. We will increase the number of issues per year from 10 to 12 (without increasing the subscription price) and grow from 60 pages of editorial content to more than 70. In January, also, look for a new, more timely and comprehensive website.

Change is inevitable in our business, but our mission, at least, won't change. *Technology Review* and its website will continue to be the first to describe emerging technologies and explain their impact. But under Jason's leadership, you will get more for your dollar and more for your mind. **R. Bruce Journey**

NEXT ISSUE

Technology of War
The Iraq War was supposed to be the most technically advanced, sensor-enabled campaign in history. But did advanced sensing and networking technologies transform the U.S. military? The answer will provide critical clues to the future of war and effective fighting forces.

Human Genome Project, Act Two
Why hasn't the genome revolution yielded better, more affordable drugs? Go inside the National Institutes of Health's new initiative to bridge the gap between genomic science and drug development.

Election Preview
New voting technology will no doubt affect this year's presidential election. A number of experts, including Paul Starr, professor of sociology at Princeton University, and Kim Zetter, an award-winning journalist, predict how.

Nanotech's Premiere
You may be surprised to learn that nanotechnology's first large commercial payoff will be coming soon to a television near you—and wait until you find out who's doing it.

Power MEMs
Batteries are expensive and heavy and constantly need recharging. A far better solution could be tiny electricity-producing machines that are now emerging from the lab.

Demo
Visit one of only a few facilities in the United States equipped to examine patients with a magnetoencephalography (MEG) machine, which measures the minute magnetic fields generated by brain cells. See how it's used to locate the structures in the brain responsible for epileptic seizures.

And more…

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PUBLISHER AND CEO
R. Bruce Journey
bruce.journey@technologyreview.com

EXECUTIVE VICE PRESIDENT AND COO Martha Connors
martha.connors@technologyreview.com

CORPORATE

VICE PRESIDENT OF BUSINESS DEVELOPMENT	J. R. "Matt" Mattox matt.mattox@technologyreview.com
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FRANCE: 612-9362-1414	Philippe Marquezy	philippe.marquezy@espacequadri.com
GERMANY: 49-511-5352-761	Karl-Heinz Piotrowski	karl-heinz.piotrowski@heise.de
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1
IBM

"Will these new [nanotech] solar cells be another environmental pollutant—the asbestos of the future?"

SOLAR REVOLUTION

IT WILL BE INTERESTING TO SEE HOW versatile and inexpensive the materials mentioned in your article "Solar-Cell Roll-out" (*TR* July/August 2004) can become. Assuming that the technology seamlessly replaces outdated and less valuable building materials, anybody could be a power-generating entity. The social implications are huge. Energy would be cheap. However, if this technology were to find its niche quickly, it could raise other problems. Given the potential toxicity of fullerenes and other nanoparticles to animals and humans, will these new solar cells be another environmental pollutant—the asbestos of the future? Once again, technology enables, but what exactly it enables is the million-dollar question.

Brandon Todd
Wheaton, IL

SOME MONTHS, *TECHNOLOGY REVIEW* seems like it's still 1999, in the heart of the technohypebubble. Like this month, when we're told that breakthroughs in nanotech will let our cell phones be powered by the sun. It is unfortunate that most people keep their phones in their pockets, in buildings, where the sun is somewhat dimmed.

Greg Kochanski
Oxford, England

PHONE CONTROL

YOUR ARTICLE "A REMOTE CONTROL FOR Your Life" (*TR* July/August 2004) shows that DoCoMo is indeed ahead of other companies. Its approach toward ubiquitous computing with a phone as a personal controller to all computers is a good step toward digital convergence. The privacy issue can be addressed by some further improvement. Then we will have a people-oriented universal communication system, and we will see the real big bang, or rather, big boom.

Hengning Wu
Reston, VA

TURNING THE CELL PHONE INTO A "universal remote," as DoCoMo is attempting to do, is a fascinating concept. There seem to be so many applications that would change how people function every day. But what if you lose your device? Not only are you without an imperative tool, you are also at risk for identity theft on a whole new level. What kind of systems are in place to react when a loss occurs?

Sarah Bixler
New York, NY

Charles Mann responds: The basic answer is that you call DoCoMo and it instantly suspends your phone service. This also cuts off all other services in the phone, because everything is channeled through DoCoMo. DoCoMo claims that it has done studies that show people are far more likely to call the phone company to cancel their service when they lose their phones than they are to call all their credit card issuers when they lose their wallets. What DoCoMo would really like to have is a system wherein people charged their cards with, say, $40 and then spent it like cash, but company officials thought customers would want transaction records. They are currently trying out various combinations to see what people will accept.

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TALL TOWERS

YOUR ARTICLE "THE WORLD'S TALLEST Building (for Now)" (*TR* July/August 2004) was very interesting. I live in Dubai and am not sure about the height of the Burj Dubai building, reported in the article as between 560 and 600 meters. Just last week, I read in a local newspaper that the true height of this building is between 750 and 800 meters. That article quoted companies that had access to the proposals submitted for the project. Clearly, Dubai is very keen to acquire the title of having the world's tallest building. That may be why it wants to keep the true height of the building a secret.

Nizam Tahir
Dubai, United Arab Emirates

SERENDIPITOUS MINDS

MICHAEL SCHRAGE'S COLUMN "PREPARED Minds Favor Chance" (*TR* July/August 2004) spotlights the competitive advantage that economies of scale afford large corporations in search of disruptive innovations. Unfortunately, we don't all work for a Merck. Luckily, Schrage has touched upon an important principle that anyone can use in search of new ideas. New ideas can best be generated through a systematic exposure to a broad, albeit shallow, range of information. The "prepared mind" takes specific steps to make this happen, one of which is likely to be skimming *Technology Review* each month to see what ideas are in various embryonic forms of development. Schrage has reminded us, yet again, of Linus Pauling's great dictum: the best way to have a good idea is to have lots of ideas.

Eric A. Sohn
Stamford, CT

Faux floods destroy Manhattan in *The Day after Tomorrow*.

VIRTUAL WATER WORLD

EVERYONE KNOWS WHAT WATER LOOKS LIKE. BUT SIMULATING IT DIGITALLY FOR the big screen can be tricky and time-consuming. At Digital Domain in Venice, CA, computer scientists Doug Roble and Nafees bin Zafar and their special-effects team have developed software that quickly creates large-scale, high-resolution water animations. Enter initial conditions of depth, volume, shape, and speed, and the software uses advanced mathematics to model a fluid's surfaces, realistically capturing phenomena such as complex currents and water swirling around buildings and people. An early version of the software was used to create the largest water simulation in a film to date: the flood in this summer's *The Day after Tomorrow*. The latest version takes five to 10 minutes to generate each frame—one-third the time needed just a year ago, and with only one-quarter the memory. Roble says the software is now being used to do visual effects in two feature films due out in 2005.

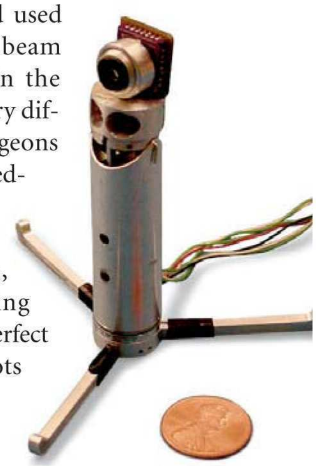
POWER DRUGS

Mitochondria are key targets for drugs.

PROBLEMS WITH MITOCHONDRIA—CELLS' TINY energy-producing units—can cause illnesses as diverse as cancer and Parkinson's disease. Volkmar Weissig, a pharmaceutical scientist at Northeastern University, says he's devised the first drug delivery system that can shuttle a drug through a cell to target its mitochondria. Weissig coats drugs in a common antibacterial compound; the positively charged coating is attracted to the mitochondria, which are the most negatively charged parts of the cell. In a recent experiment with mice, Weissig found that tumors treated with the coated version of the cancer drug Taxol grew only half as much as those treated with the uncoated drug. Weissig says he could also use the approach to shuttle DNA to the mitochondria, a possible basis for gene therapy to correct mutations in mitochondrial DNA—which have been implicated in neurological diseases such as Parkinson's and Alzheimer's. A Boston startup company, MitoVec, plans to couple Weissig's technology with several existing cancer drugs and begin testing it in humans in two to three years.

ROBOSURGEON

ACCIDENT VICTIMS AND INJURED SOLdiers could be saved at the scene by tiny wheeled robots slipped into their abdomens and controlled by surgeons hundreds of kilometers away. In experiments conducted at the University of Nebraska, the robots carried cameras fitted with light-emitting diodes to illuminate the abdomens of pigs and used radio transceivers to beam back video images. In the field, robots would carry different tools so that surgeons could stop internal bleeding—the main cause of traumatic death—by either clamping, clotting, or cauterizing wounds. "We want to perfect a family of little robots that paramedics can insert into a patient through a small incision," says University of Nebraska-Lincoln mechanical engineer Shane Farritor, who is working with Dmitry Oleynikov of the University of Nebraska Medical Center. Farritor expects finished prototypes within two years.



Camera-wielding robots aid emergency surgery.

TRANSLATION IN MOTION

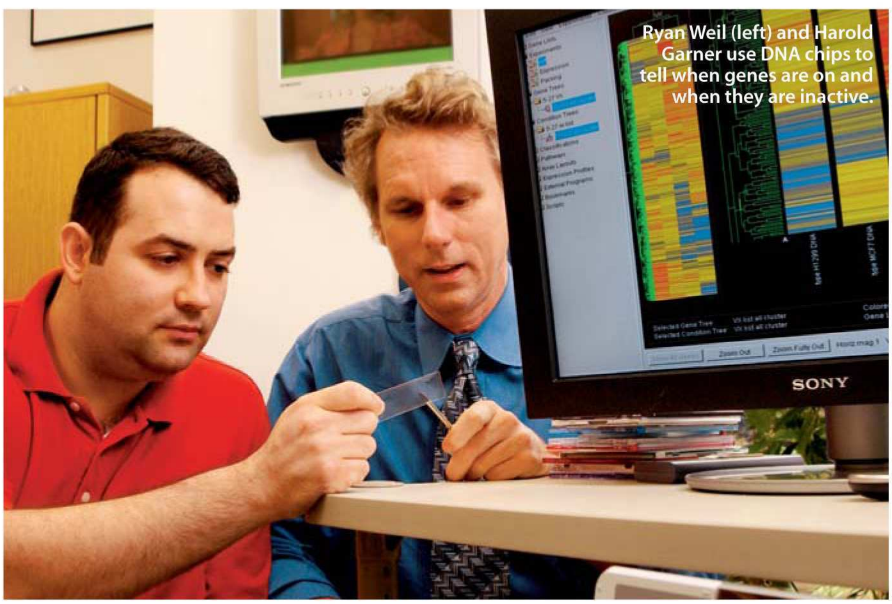
Your colleague in Germany thumb-types "Wir benötigen fünf tausend Kondensatoren bis zum Dienstag" into her cell phone. Three seconds later and nine time zones away, the translated text pops up on your Blackberry: "We need five thousand capacitors by Tuesday." A system that makes this possible—by melding mobile text messaging and e-mail with the latest in machine translation—will be available to wireless subscribers this fall from New York City–based Transclick. For $30 per user per month, multinational corporations will be able to install the software on their employees' PDAs and smart phones. Workers will then upload country-to-country text messages or e-mails to Transclick's servers, which render translations using dictionaries customized to their users' lines of business—say, law or pharmaceuticals.

COURTESY OF VOLKMAR WEISSIG (POWER DRUGS); COURTESY OF SHANE FARRITOR (ROBOSURGEON); COURTESY OF DOUG ROBLE (WATER WORLD)

PORTABLE PATHFINDER

A simple interface helps people navigate to their choice of destinations.

FOR MANY PEOPLE WITH BRAIN injuries, mental retardation, or Alzheimer's disease, getting lost or disoriented is a common and distressing experience. At the University of Washington, computer scientist Henry Kautz's team has developed a system that uses cell phones to monitor users' whereabouts and help keep them on track. The phone, equipped with a GPS receiver that gauges its location, communicates wirelessly with a PC running novel artificial-intelligence software. Based on about three weeks of data, the software learns to predict daily behavior patterns, such as which bus a user takes. Then, if the system thinks the user is, say, getting off at the wrong bus stop, the phone sounds an alert and displays a text prompt on the screen—including directions for getting home. Kautz's team plans to do tests next spring, together with University of Washington researchers in rehabilitation medicine. The software could be on the market within two years.



Ryan Weil (left) and Harold Garner use DNA chips to tell when genes are on and when they are inactive.

ALL WOUND UP

FIGURING OUT WHICH GENES ARE ACTIVE AND WHICH AREN'T—IN, SAY, AN organ or a group of cells—is critical for both basic biological research and the development of treatments for diseases like cancer. Researchers at the University of Texas Southwestern Medical Center have developed a way to simultaneously assess, for a given biological sample, the activity of all the genes in the genome, based on how tightly their DNA is wound. DNA spends much of its time coiled up; when a gene is turned on, its segment of the coil unwinds. Biophysicist Harold Garner says he has devised a way to separate coiled DNA from DNA that's "loose and free." His team then uses DNA microarrays to determine which genes are in the open group—and therefore active. The technique could help uncover the secrets of a host of diseases, Garner says. The researchers, for instance, are using it to find out how cancer drugs affect gene activity. "This will allow us to hopefully tune some of those drugs and identify new drugs that may work better," Garner says.

COURTESY OF RYAN WEIL (ALL WOUND UP); COURTESY OF ANDREW KAHNG (CALL FORWARDING); COURTESY OF HENRY KAUTZ (PATHFINDER)

RFID RELIEF

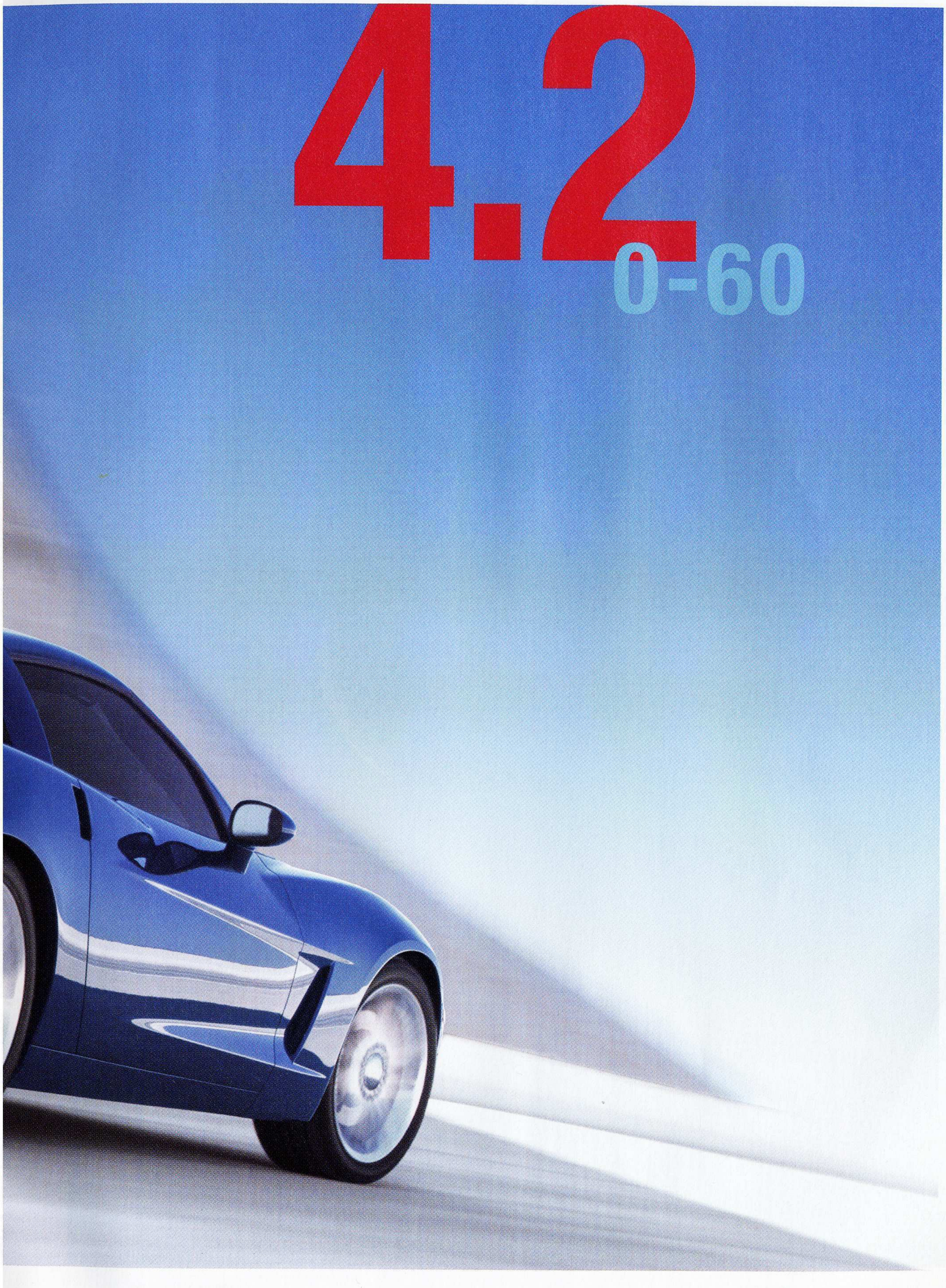
Software that should make it easier for small businesses to adopt radio frequency ID technology—without breaking the bank—is being readied for release by Dallas, TX, startup AirGate Technologies. The latest RFID tags can store product details that let companies track items from factory to warehouse to retail shelf; large organizations like Wal-Mart and the U.S. Department of Defense are rapidly implementing the technology and dragging their suppliers along with them. The problem, says AirGate CEO Michael Sheriff, is that many smaller companies that own multiple brands of RFID readers—one at the warehouse doors, another in the product-label printers, and so forth—and use multiple systems for storing product information can't afford custom software to link them all together. AirGate's one-size-fits-all software, to be unveiled next spring, acts like a universal translator. It's the first system that can take data from any RFID reader and present it intelligibly on a simple Web page or dump it into a database program.

CALL FORWARDING

IN TODAY'S MOBILE SOCIETY, IT SEEMS people are hardly ever around to answer landline phone calls. But software developed at the University of California, San Diego, lets you take those calls on any Internet-connected device. A system devised by Andrew Kahng and Puneet Sharma enables a PC to digitize a phone call coming in on a landline and forward it via the Internet to a Wi-Fi-enabled cell phone, a PDA, or even another computer, so long as it's also running the software. Outgoing calls made from the remote device can also be routed back through the landline, allowing a user to, for instance, avoid long-distance charges. Kahng and Sharma plan to commercialize the technology early next year.

Software turns a PDA into an Internet phone.


RJP 263
CORVETTE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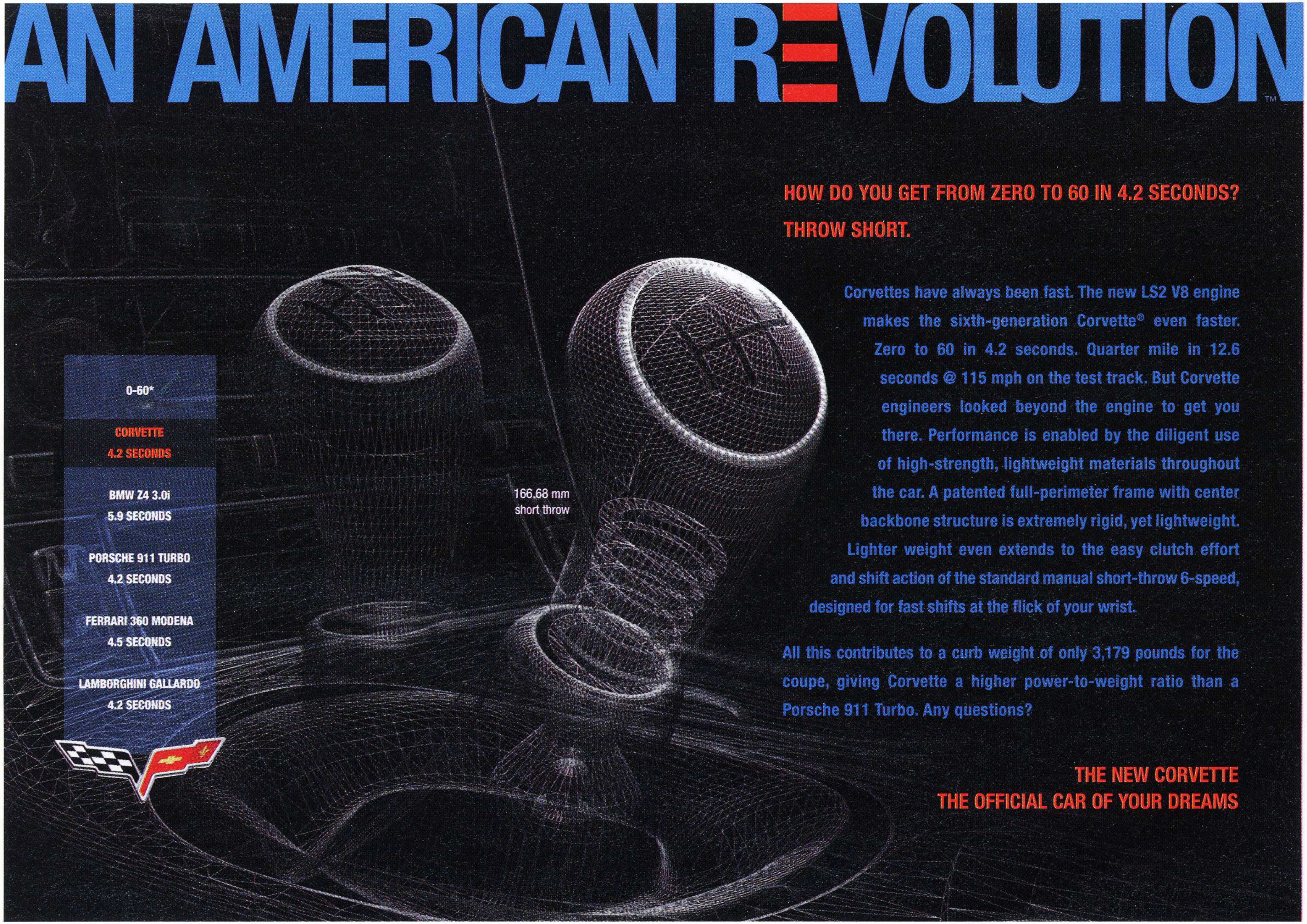
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Great Expectations

"THE COMPUTER OF THE FUTURE: IF STAN WILLIAMS of HP has his way, it will be a computer that assembles itself—in a beaker." "Mining the Genome for New Drugs." "Micromachines—The Next Big Thing." ▪ Intrigued? Actually, these are all five-year-old stories, featured on the cover of the September/October 1999 issue of *Technology Review*. ▪ The days of the tech bubble are gone forever, but the cover stories linger on. Those precise topics could reappear this year or next with little fear of editorial embarrassment. It's not even snarky to say so; it would be truly astonishing if the biggest technology challenges of 1999 weren't challenges today. But beyond the old theme of *plus ça change*, these hardy perennials contain critical insights for innovators—if they know how to read (and reread) them.

Those insights have less to do with the technologies themselves than with the *expectations* they created, induced, and excited. Look at old issues of *Technology Review* or *Wired*, and you'll swiftly realize that the past *isn't* prologue: it's a turbulent world of heady speculations and unfulfilled promises. Those "promises" are indispensable elements of the innovation ecosystem. When artfully calibrated against actual progress, they keep markets salivating and investment—of both financial and human capital—flowing. Reviewing the headlines of times past can help innovators constructively fine-tune that balance around their own inventions.

In technology journalism, the pattern is almost always the same: the promise of a technical invention provokes a swirl of speculation around its potential impact if and when it reaches the market. In other words, novel inventions breed bold intentions. But exactly what happens to Intel if computers start self-assembling in beakers? Which new drugs will be profitably brought to the surface by genome mining? How micro or nano will those machines actually become on their way to being the Next Big Thing? We don't know the answers; we can't know. All we can say with any confidence is that inventors have fervent expectations for progress in their fields. They're investing their efforts and ingenuity accordingly.

Innovators must maintain an artful balance between promises and actual progress.

Why is this so important? Because successful innovation—seeing invention through to adoption—isn't just about managing technical breakthroughs; it's about managing people's expectations. Always. Credibly aligning technical progress with past promises is the central challenge confronting most innovators.

By far the most successful example is Moore's Law. For almost 40 years, circuit densities *have* doubled every 18 to 24 months, just as Intel cofounder Gordon Moore predicted. In this case, the prediction itself, and the pace the semiconductor industry has historically set for itself in order to keep up with the prediction, have seamlessly blended into one. Moore's Law is as much a sustaining ideology as an engineering insight.

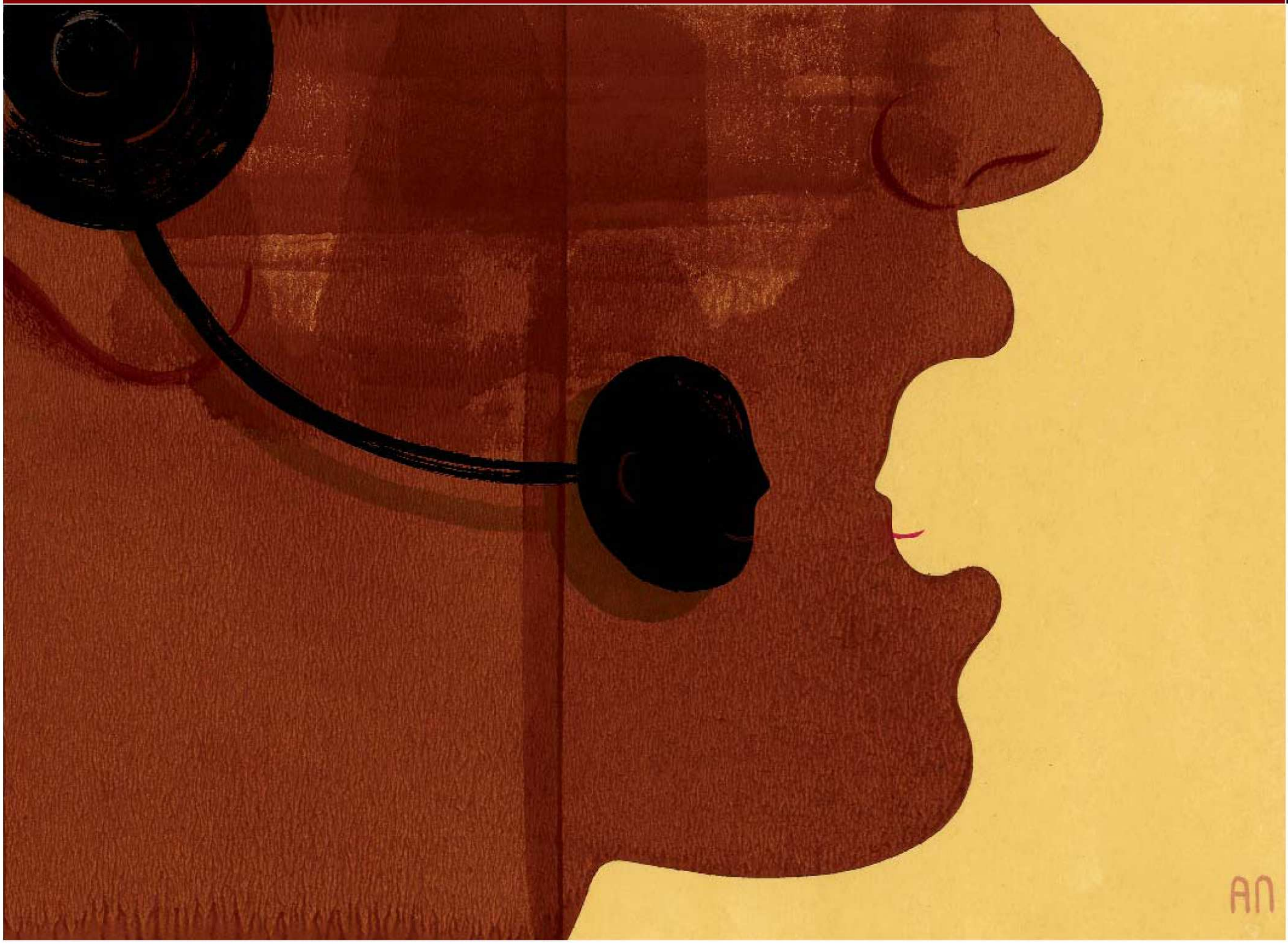
But this magnificent exception proves the rule. What does recent history teach about the marriage of technical prediction and market expectation? Reread the September/October 1999 *Technology Review*, and the answer is obvious: innovators stink at managing expectations. They're either overly optimistic or unduly pessimistic. They haven't a clue what new costs their innovations will impose on potential users. They have no credible way to assess what needs will be most important to those users three years hence.

But the reason innovators should read these tales of technologies past is emphatically not to "learn from the lessons of history." Rather, it's to see how expectations have changed over time. What expectations were innovators trying to create? How fast are those expectations changing, compared to market conditions? Determining this "expectations calculus" is essential to managing innovation.

Take the story of gallium arsenide. For years, this exotic material was promoted in the press as a replacement for silicon in integrated circuits, with proponents touting its superior speed. But gallium arsenide is expensive, and Moore's Law had long since trained the computing market to expect continual cost *reductions*, not increases. In this case, a careful analysis of the hype versus the economics would have nudged innovators back toward silicon or toward niches where gallium arsenide might be worth its significantly higher cost. In fact, that's exactly what happened: gallium arsenide has become a key material in high-speed chips for cell phones and other telecommunications devices.

The history of technology predictions is a resource to be mined, not a pile of failed futurology to lampoon. Don't save past issues of *Technology Review* to see what the magazine got right or wrong; treat *TR* and its conceptual cohorts as media that measure the expectations tomorrow's innovators need to understand in order to exploit. TR

A researcher and consultant on innovation economics, Michael Schrage is the author of *Serious Play* (Harvard Business School Press, 2000).



ALEX NABAUM

Phones Pick Up Language

Faster chips and better software help mobile devices recognize speech. **BY MARA E. VATZ**

CELL PHONES AND WIRELESS PDAs have one perennial problem: either no keyboard or a very small one. That makes typing anything more than a phone number a tedious, fumbling task. But a solution is on the way: mobile devices that are adept at recognizing spoken language.

Some cell phones already use speech recognition as an alternative to keypad entry for simple tasks such as dialing a number, but someday soon you may also find yourself dictating a text message into your phone, asking your car for directions, or telling your MP3 player that you want to listen to the Beatles. Indeed, today's high-end cell phones are capable of running sophisticated speech recognition software that could eventually mean the end of pecking at keyboards. "The fundamental problem of inputting information into mobile devices is the interface, and voice overcomes that," says Rich Geruson, CEO of VoiceSignal, a speech technology company based in Woburn, MA.

While companies like IBM and Dragon Systems (now part of Peabody, MA-based ScanSoft) have been selling desktop speech recognition software for more than a decade, mobile devices with even limited speech recognition abilities appeared only several years ago. And until now, such devices have largely been "speaker dependent"—meaning they work well only for their principal users and have to be trained to recognize individual words.

Faster processors and more efficient software, however, are enabling new

speaker-independent systems that can recognize the speech of any user and require no training. These systems can discern thousands, rather than dozens, of names and are designed to work even when the speaker is in a noisy environment, such as the front seat of a speeding car.

For the engineers at VoiceSignal, the key to this advance was a shift in focus from accuracy to efficiency. The highly accurate speech recognition algorithms designed for desktop computers are too complex to run on mobile devices. Traditional algorithms for mobile devices required less processing power, but because they worked by matching the sound wave of an entire word to a sound wave stored in a device's memory, they were limited to a small vocabulary.

Instead of storing an entire sound wave for each word in its lexicon, VoiceSignal's new system stores information about phonemes—the smallest units of recognizable speech. Every phoneme can be described according to a set of acoustic parameters, such as pitch. The software measures a user's utterances along these parameters and then looks for words that match. Parameter values take up less memory than audio files, so the software can handle a larger vocabulary without requiring any additional storage space.

And that's opening up applications beyond simple voice dialing. For example, VoiceSignal offers software that lets users jump to any node of a cell phone's menu with a single utterance. "If you try to send a [text] message on your phone right now, you have to do about ten clicks just to get to the message space," says Geruson. "With our technology, you just say, 'Send message to John Smith's mobile,' and your cursor is flashing and ready to go." The first phone with this capability was released in August. Within six months the company also plans to release software for phones that lets users dictate text messages and e-mails, which Geruson anticipates will be particularly useful in Asia. "If you think it's hard to input into a keyboard in Western or Latin languages, think about the problem in Japan or China, where you have thousands of characters," he says.

Researchers at ScanSoft, meanwhile, are putting speech recognition to use in cars. A car kit with a built-in microphone, speakerphone, and ScanSoft speech engine provides motorists with a hands-free interface for their cell phones. A phone equipped with a Bluetooth wireless transmitter can be placed anywhere in a car, and drivers can use voice commands to dial, accept or reject calls, adjust the volume, and control menu options, all without taking their hands off the wheel or their eyes off the road.

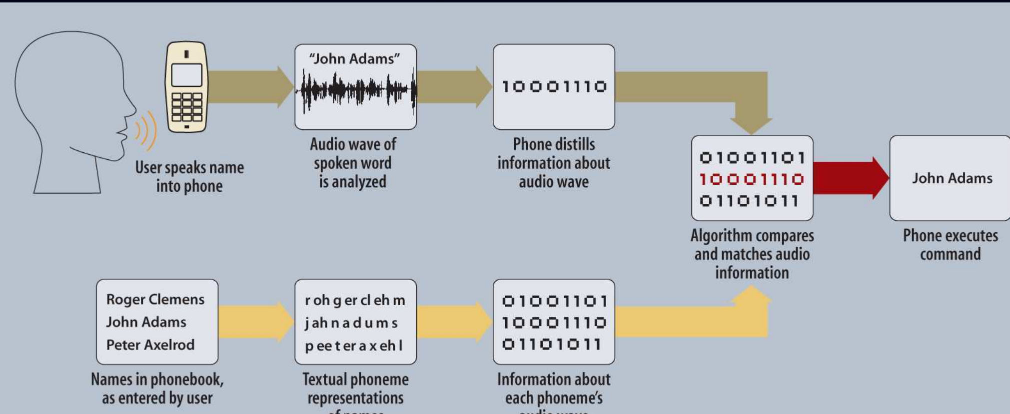
While the wireless industry has been the first to embrace speech recognition, makers of consumer electronics appear to be close behind. At the Mitsubishi Electric Research Laboratories in Cambridge, MA, researchers are developing software that enlists speech to simplify the task of searching for information. Rather than scrolling through 10,000 MP3 songs on a handheld device, for instance, a user could select a single song just by saying its name—or that of a band or album. "We decided one of the things [speech] was good at was choosing," says Mitsubishi speech technology researcher Peter Wolf.

Despite these advances, however, it remains to be seen how widely speech recognition will be adopted. Phone users may feel uncomfortable dictating personal e-mails in public. And they may always want keyboards for entering sensitive information such as credit card numbers. But Geruson predicts that the technology will eventually transform the way people use mobile devices. As a few early adopters take to the technology, he says, "it will catch on, and then it will be everywhere." TR

"Speaker dependent" speech recognition algorithms are giving way to software that can understand any user, with no training.

YOUR WORD IS ITS COMMAND

Speech recognition software for the latest cell phones works by comparing information about a sound wave—such as pitch and duration—to stored parameters for all the words in its vocabulary. If the software finds a matching word, it prompts a predefined action, such as dialing a number.



SOURCE: VOICESIGNAL

HARDWARE

Pocket Projectors

Imagine that your mobile phone or PDA had a display the size of a laptop's but still fit snugly in your pocket. Hardware engineers at several companies are working on miniature video projectors that promise just that. Using projection, "you can make an image larger than the size of the device you carry," says research scientist Ramesh Raskar of the Mitsubishi Electric Research Laboratories in Cambridge, MA.

Key to the new projectors are lights small enough to squeeze into a PDA-sized gadget but bright enough to display crisp images. Lumileds Lighting in San Jose, CA, has built a prototype projector roughly the size of a pocket camera that employs small, powerful light-emitting diodes (LEDs) to throw an image the size and brightness of a laptop's screen onto any white surface. The Mitsubishi lab is using LEDs to build an even smaller projector, about the length and width of a credit card.

The first pocket-sized projectors, available within the next three years, will probably be stand-alone accessories priced at $300 to $900, the companies predict, but the ultimate goal is to fit them inside handhelds. And with camera phone owners snapping photos by the thousands—manufacturers will ship an estimated 800 million camera phones by 2007—a built-in projector that displays photos in larger formats could be a big draw for cellular customers.

Beyond that, says Adrian Cable, director of Light Blue Optics, a spinoff of the University of Cambridge in England that is developing a holographic miniprojector, "You can imagine a video analogue of the iPod that you could download DVDs into" and use as a portable cinema projector. And that would be infinitely cooler than a pocket laser pointer. **Charles Q. Choi**

A mock-up of Lumileds's prototype projector

MEDICINE

Fighting Infections with Data

Every year, two million Americans contract infections in hospitals, and about 90,000 of them die as a result. Despite the severity of this quiet epidemic, physicians have no systematic way to quickly and effectively identify spreading hospital infections. Now a small but growing number of U.S. hospitals are adopting data-mining technologies widely used in other industries to alert doctors to problems they might otherwise miss.

One company helping hospitals connect the dots is MedMined of Birmingham, AL, which has sold its data analysis services to more than 80 hospitals since physician and computer scientist Stephen Brossette founded it in 2000. Hospitals transmit encrypted data from patient records and lab tests to MedMined, which then uses its data-mining algorithms to tease out unusual patterns and correlations. At first, only the most computerized and technologically savvy hospitals were interested, but "now we're seeing more of a mainstream push," says Brossette, the company's president and chief technology officer. One incentive: increased public scrutiny of hospital-acquired infections. Illinois, Pennsylvania, and Missouri have passed laws requiring hospitals to publicly reveal their infection rates, and similar bills are pending in Florida and California.

MedMined and competitors such as Cereplex and Theradoc *(see "Computerized Germ Catchers," below)* also track emergency-room and outpatient-clinic data to look for community outbreaks and bioterrorism events. Automating disease surveillance "is going to be hugely beneficial for patient care," says Jerome Tokars of the Centers for Disease Control and Prevention in Atlanta. "Instead of collecting and counting data, personnel can start doing more prevention of hospital-acquired infections."

One concern about the technology, says Robert Weinstein, chair of infectious disease at the John H. Stroger Jr. Hospital of Cook County in Chicago, is that it may send doctors chasing after too many false positives—seeming clusters of infections that turn out to be random statistical anomalies. Even so, most infection control specialists agree that they need help from computers in crunching the mountains of patient data that may conceal evidence of an impending outbreak. **Corie Lok**

COMPUTERIZED GERM CATCHERS

COMPANY	TECHNOLOGY/MILESTONES
Cereplex (Gaithersburg, MD)	Looks for unusual infection patterns and identifies patients needing changes in therapy; has data analysis contracts with 11 U.S. hospitals
Theradoc (Salt Lake City, UT)	Software on hospital servers mines patient data for trends in infections and suggests courses of action for particular patients; sold to 12 U.S. hospitals
Vecna Technologies (College Park, MD)	Data-mining software for infection control; in tests at three Boston hospitals

COURTESY OF LUMILEDS LIGHTING

INTERNET

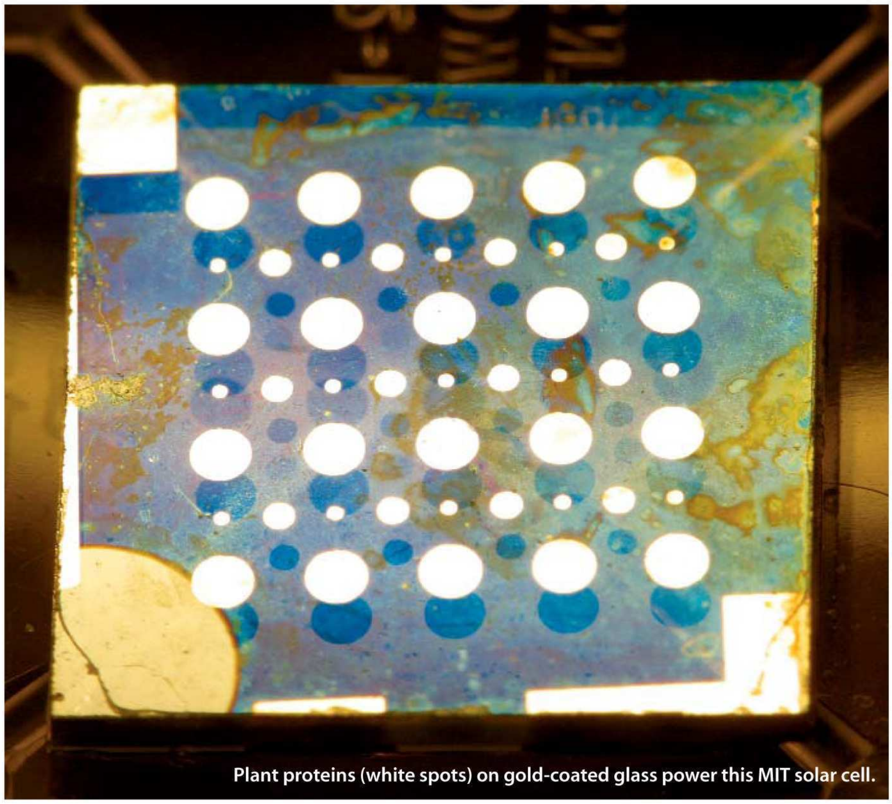
Talking Spam

It might be a nightmare that few of us want to imagine. But as more people abandon traditional phone lines and start placing calls over the Internet, an explosion of voice-mail spam is a real possibility, telecommunications experts say. To contain that explosion, engineers at Qovia, a voice-over-Internet-Protocol (VoIP) management company in Frederick, MD, have developed a technology that may shut up voice spam before it gets started.

Internet technology makes it easy for a single "caller" to send voice messages to thousands of people's VoIP mailboxes. Indeed, last fall, Qovia engineers managed to write software for two major types of VoIP systems that sent voice messages to 1,000 targets per minute in simulations—the first known demonstration of spam over Internet telephony, or SPIT. Though no real-life cases of SPIT have been documented, that's largely because there aren't enough VoIP users to make it worthwhile for spammers, says Winn Schwartau, president of Interpact, a security consulting company in Seminole, FL.

That's changing rapidly, though. In 2003, there were only about 131,000 residential VoIP subscribers, according to the Yankee Group, a Boston-based communications research firm. By 2008, that number is expected to skyrocket to more than 17.5 million, roughly the number of people who were using e-mail when spam took off around 1995. The result could be an at least temporary resurgence of telemarketing; the Federal Trade Commission's do-not-call registry does not restrict calls made over the Internet.

But by monitoring factors such as the length of calls and the rate at which calls are being made from particular Internet addresses, Qovia's software can identify and block up to 95 percent of SPIT before it reaches its intended recipients, says chief technology officer Choon Shim. The company plans to incorporate the technology into its VoIP security software later this year, and if Qovia customers such as Nortel Networks build the software into their systems, SPIT may be one frustration we never have to face. **Erika Jonietz**



Plant proteins (white spots) on gold-coated glass power this MIT solar cell.

COURTESY OF PATRICK KILEY

ENERGY

Spinach Power

IT MAY SOUND LIKE SOMETHING OUT of a Popeye cartoon, but MIT researchers are building a promising solar cell from spinach. In their Cambridge lab, bioengineer Shuguang Zhang and electrical engineer Marc Baldo shine a laser beam on a chip the size of a postage stamp. Out of a wire electrode hooked to the chip comes electricity—a trickle now, but one day, perhaps, enough to power a cell phone or laptop. Instead of the silicon found in most solar cells, however, this chip uses proteins from plants that have evolved over millions of years to turn sunlight into usable energy.

The advance "is of tremendous importance," says Peter Peumans, an expert on organic electronics at Stanford University, because solar cells that draw on plants' natural photosynthetic ability could eventually be lighter, cheaper, and easier to repair than their conventional cousins.

Biological cells removed from plants and connected to electronic hardware typically die within hours. But Zhang and Baldo, collaborating with the University of Tennessee and the U.S. Naval Research Laboratory, took wholesale spinach and harvested just the proteins that absorb photons and generate free electrons during the process of photosynthesis. The researchers bathed the proteins with detergent-like molecules that would keep them working properly on a dry surface for weeks. They then placed the proteins on a gold-coated glass substrate and deposited a semiconductor layer on top to collect electricity.

So far, the chip's energy efficiency is far lower than that of existing solar cells. But "extensions of these methods could produce very important future energy conversion technologies," says MIT chemist Timothy Swager. To ratchet up the chip's efficiency enough that it could power a mobile device, says Zhang, the researchers plan to increase the area of its light-absorbing surface by building layers of proteins on wavy substrates. Zhang predicts the technology could be used commercially in five years. **Gregory T. Huang**

ELECTIONS

Concerns Grow over E-Voting

If quirky ATM machines randomly erased the accounts of 1 percent of their patrons, they'd quickly be taken out of service. Yet touch-screen electronic-voting machines that recorded no vote for 1 percent of voters in Florida's Democratic primary in March are set to be used again in nearly a quarter of the state's 67 counties. And Florida is hardly alone in switching to this relatively untested technology: 20 percent of the nation's 3,114 counties will use electronic voting machines in November. That rate of adoption alarms some experts. "We're not ready," warns Douglas W. Jones, a computer scientist at the University of Iowa in Iowa City. "I'm suspicious if we'll ever be ready."

In Florida's case, it's unlikely that one in a hundred people who went into electronic polling booths in March deliberately cast no vote, given that voters using ballots read by optical scanners—like those used to score standardized tests—cast far fewer so-called undervotes. But if the machines were at fault, no one will ever know for sure, since they produced no paper trail or independently auditable record. And that's one of the biggest concerns about current electronic voting technology, says Martha Mahoney, a professor of law at the University of Miami and a member of the Miami-Dade Election Reform Coalition, an activist group. The machines "lack transparency for the voter," she says. "The voter casts a ballot but doesn't see how the ballot is recorded."

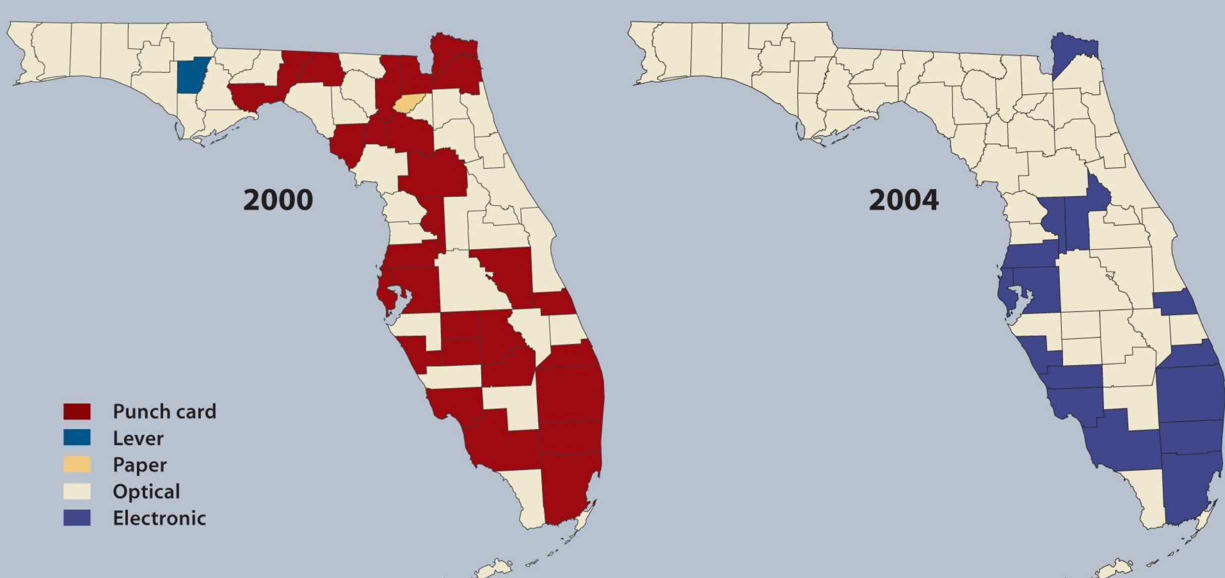
Computer scientists would relish the opportunity to help guard against errors or tampering by scrutinizing these electronic voting machines for bugs and vulnerabilities to hacking. But most electronic voting machines run proprietary software, which manufacturers are reluctant to release to any except their own testing authorities. Consequently, there is no independent verification that the code works as advertised and that nobody has tampered with it, says Michael Wertheimer, a cryptologist at computer consulting firm RABA Technologies in Columbia, MD.

Some experts contend there are ways to make electronic elections safer while still maintaining voter anonymity. Ted Selker, a professor at the MIT Media Lab who directs the Caltech-MIT Voting Technology Project, points out that many electronic voting machines are already equipped with headphones to help vision-impaired voters. This feature, Selker says, could be used to verify all voters' ballots; software independent of the voting machine could read off the name of each candidate a voter selects, and a tape of the day's votes could serve as an independent record in contested elections.

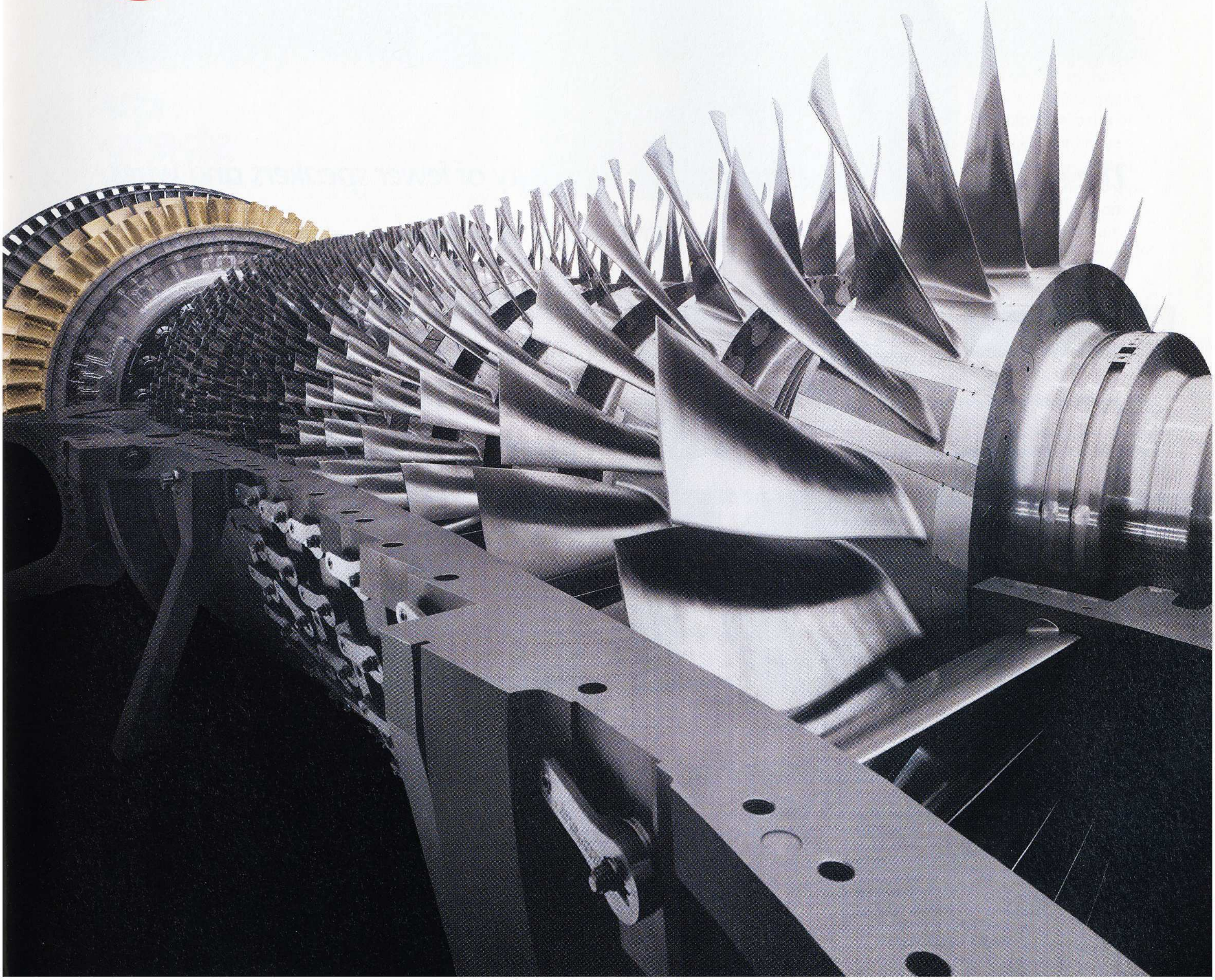
But while ideas like these could help make future election results more trustworthy, it's probably too late to replace or modify the equipment counties will put into action on November 2. Indeed, laments Wertheimer, with so little time remaining and so much money already spent on new voting equipment, many election officials don't want to hear that the technology may be flawed. "With every day that passes," he says, "people will say, 'So what? We can't change anything before the election.'" **Katherine Snoda Ryan**

SWITCHING SYSTEMS IN THE SUNSHINE STATE

Many of the Florida counties that used punch-card voting systems in the 2000 presidential election (crimson, below left) have turned to electronic voting machines instead (violet, below right). The rest switched to systems using optical readers.



SOURCE: ELECTION DATA SERVICES



NEW

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settlement

In a bid to resolve two lingering legal disputes, **Google** has given rival search site **Yahoo** 2.7 million shares of its stock, or about 1 percent of its total shares. One dispute involved a 2000 agreement to let Yahoo purchase 3.7 million shares; Google claimed that a provision in the agreement reduced its obligation to only 1.2 million shares. The other tussle was over Google software that, according to Yahoo, infringed on patents Yahoo holds on techniques for linking ads to specific keywords.

play»

Doom 3, one of the year's most anticipated video games, has been zooming off shelves since its August 3 debut. Available for PCs, Doom 3 is the creation of id Software of Mesquite, TX, whose original Doom popularized the "first-person shooter" genre in 1993. Id plans to profit not only by selling copies of the game—which deals with a demonic invasion of an underground Mars base—but by letting other game developers license the 3-D graphics engine that provides the game's gory graphics.

advance

NASA has been pushing its supercomputers to the limit this year with massive simulations aimed at returning the remaining space shuttles to flight. Now the space agency is working with Mountain View, CA-based computer manufacturer **Silicon Graphics** and **Intel** to build a machine that will increase the agency's overall supercomputing capacity by a factor of 10. Nicknamed Project Columbia, the computer will contain 10,240 separate Intel Itanium processors—more than any other currently operating supercomputer.

upgrade

In its first major round of operating-system improvements since it introduced Windows XP in 2001, Microsoft released the long-awaited **Windows XP Service Pack 2** in August. Going well beyond the typical software fix, the 80-megabyte update overhauls both Windows and the Internet Explorer browser, providing better defenses against hacker attacks, viruses, and other malicious code.

hardware

Hewlett-Packard will become the first major computer maker to release a Linux laptop. Versions of the **HP Compaq nx5000** with the open-source operating system preinstalled will have a suggested retail price of $1,140.

Infote

web»

Publishing a weblog isn't just for the hoi polloi anymore. A growing number of technology leaders are getting into the act. A selection:

Mitch Kapor	Founder, Open Source Applications Foundation	blogs.osafoundation.org/mitch/
Tim O'Reilly	Founder and CEO, O'Reilly Media	www.oreillynet.com/weblogs/author/27
Ray Ozzie	Founder, chairman, and CEO, Groove Networks	www.ozzie.net/blog/
Jonathan Schwartz	President and chief operating officer, Sun Microsystems	blogs.sun.com/jonathan

COURTESY OF ID SOFTWARE (PLAY)

ipo

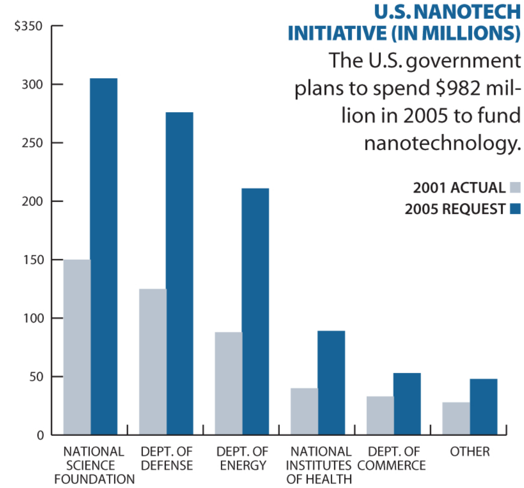
Ending its quest to be the first high-profile nanotech startup to go public, **Nanosys**, based in Palo Alto, CA, has withdrawn its planned IPO. While nanotech observers have suggested that the move was the result of waning optimism over nanotech's short-term market potential, the company cited "adverse market conditions" that it said meant it "is not advisable at this time to proceed."

collaborations

Woburn, MA-based **Nantero**, a startup developing electronic applications for carbon nanotubes, has partnered with **BAE Systems**, the large U.K. aerospace manufacturer, to work on electronic devices for advanced defense and aerospace systems. Nantero's goal is to develop high-density nonvolatile random-access storage devices based on carbon nanotubes; such devices could serve as a universal memory, replacing DRAM and flash memory. BAE says it plans to combine Nantero's know-how with its semiconductor technology.

U.S. NANOTECH INITIATIVE (IN MILLIONS)

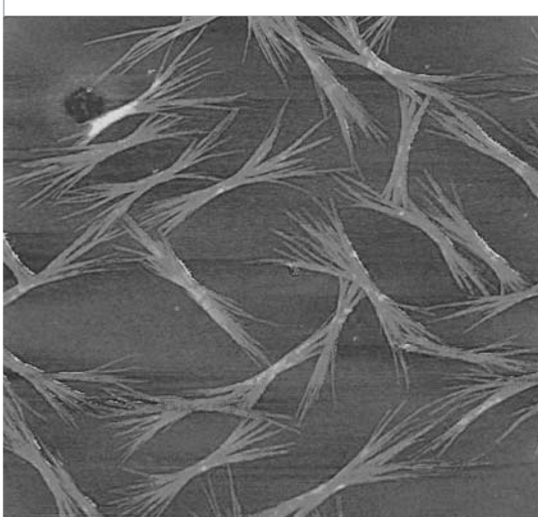
The U.S. government plans to spend $982 million in 2005 to fund nanotechnology.



Nanot

regulations

The U.K.'s **Royal Society** and **Royal Academy of Engineering** have released a study calling for a series of steps to ensure the safety of nanotechnology. Among its recommendations is a multidisciplinary center to study the toxicology and environmental impact of nanoparticles and nanotubes. The groups also recommend that the release of nanoparticles and nanotubes into the environment "be avoided as far as possible."



« advance

Teaching one of biology's basic molecules a new trick, researchers at **Purdue University** have coaxed RNA into forming three-dimensional structures (left). The hope is that RNA could one day offer a quick and easy way to make scaffolding that would, in turn, be used to construct nano devices, including tiny sensors and diagnostic chips.

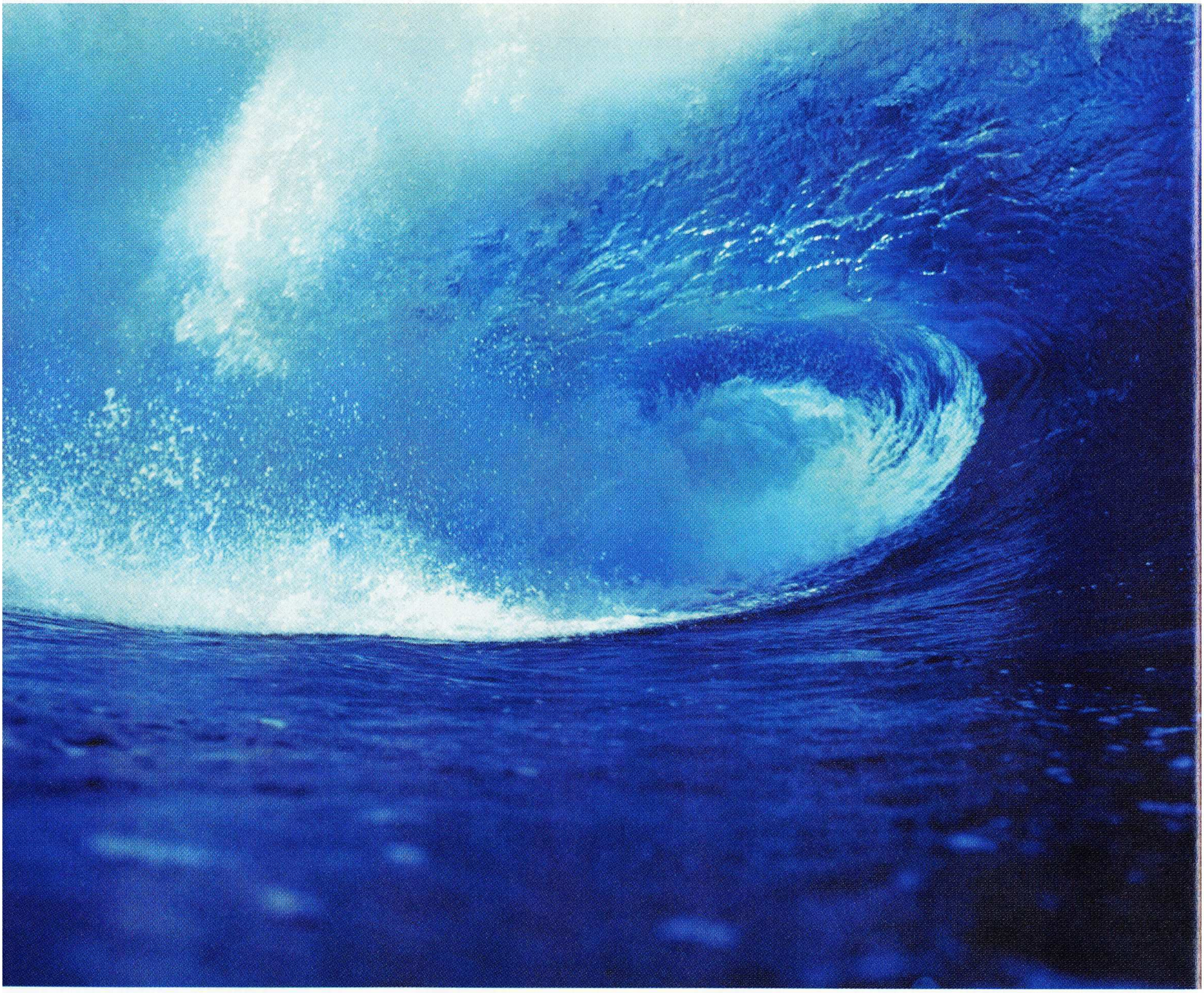
financing

Reflecting the growing interest in using nanotech for biological applications, Seattle's **Nanostring Technologies** has raised $4.3 million in venture investment. The startup aims to develop a bar-coding system for single molecules that could lead to devices 100,000 times more sensitive than existing DNA microarrays used in diagnostics and forensics. The technology was originally developed at Seattle's Institute for Systems Biology.

follow-up

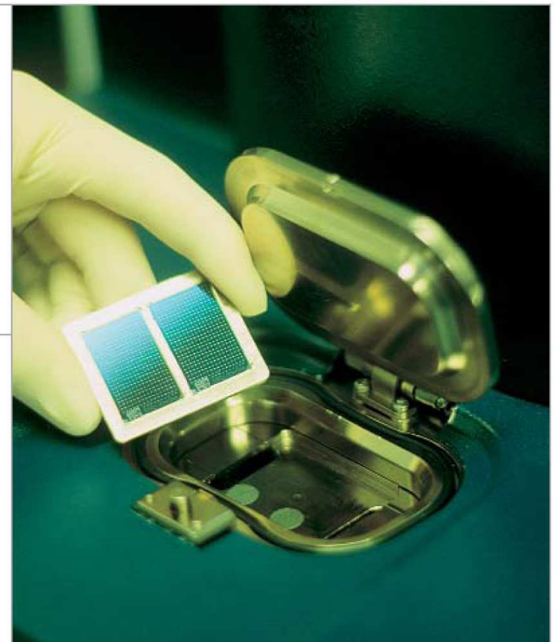
Cambrios Technologies, a San Francisco startup formerly called Semzyme, says it has secured $1.8 million in venture financing. Cambrios was cofounded by Angela Belcher, a materials scientist at MIT who has developed novel ways to make electronic materials using genetically engineered viruses and bacteria *(see "Biotech Boost for Nanoelectronics,"* TR *June 2003)*. Cambrios intends to use the technology as a way to fabricate high-quality nanoscale structures out of semiconductors, metals, ceramics and magnetic materials.

COURTESY OF PURDUE UNIVERSITY (ADVANCE); SOURCE: LUX RESEARCH (NANOTECH INITIATIVE)



milestone

Philadelphia's **Acuity Pharmaceuticals** has planned for this fall the first-ever human tests of RNA interference (RNAi), in which small pieces of RNA are used to turn off disease-causing genes. Acuity aims to test RNAi's mettle as a treatment for a severe form of age-related macular degeneration, which is a common cause of adult blindness.



follow-up

A heart-failure drug that will be marketed specifically to African Americans did so well in late-stage human tests that the tests were halted early so that volunteers in the control group could take the drug too. One of a handful of new "ethnic drugs" *(see "Genes, Medicine, and the New Race Debate," TR June 2003)*, the heart-disease treatment could be on the market a year ahead of schedule, says Michael D. Loberg, CEO of Lexington, MA-based **Nitromed**, the drug's developer.

regula-tions

Genetically engineering crops poses no unique health risks, concludes a report by a committee of the **National Academy of the Sciences**. The committee urged that the safety of all new foods—including those produced through conventional breeding—be evaluated on a case-by-case basis.

advance

Researchers at the Chinese University of Hong Kong and Boston University have found a way to detect genetic defects in fetuses by testing their mothers' blood. The technique, which could spare pregnant women invasive tests like amniocentesis, uses chip-based mass spectrometry technology from San Diego's **Sequenom** to analyze the minute amounts of fetal DNA that circulate in the maternal bloodstream.

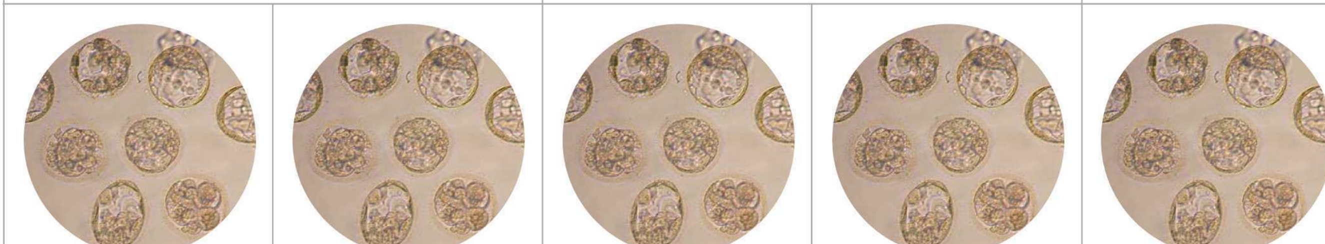
Biote

ipo

While other biotech firms were pulling planned IPOs and slashing their offering prices, Valencia, CA-based **MannKind** raised $87.5 million—more than it had originally projected. The biopharmaceutical company's lead product, an inhaler that delivers powdered insulin, is undergoing human testing.

milestone

The U.K. Human Fertilisation and Embryology Authority has granted researchers at the nonprofit **Centre for Life** in Newcastle, England, a license to use cloning techniques to create human embryos *(below)* and harvest stem cells from them. Though such cells could eventually help treat ailments such as Parkinson's disease and heart failure, those created under the license—the first of its kind in the United Kingdom—will be used for research only.



AP PHOTO/SEOUL NATIONAL UNIVERSITY (MILESTONE); COURTESY OF SEQUENOM (ADVANCE)

Panning Out

WAVES OF INVESTMENT IN NEW TECHNOLOGY ARE often likened to gold rushes in their cycles of boundless enthusiasm, frenzied activity—and disappointment for the vast majority of people for whom things don't quite pan out. Entrepreneurs bear the most risk in that they wager years of their lives (not to mention personal savings) on individual claims, whereas investors can spread their bets around in the hope that at least one promising property will make good. Even the certainty that a budding technology will change the world is no more help in making money than the certainty that there really is gold somewhere in them thar hills. The typical hundred dollars invested in Internet startups in 2000 would barely pay for a snail-mail stamp today. Clearly, transmuting raw hope into net profits requires investors and entrepreneurs to place extremely prescient and/or damn lucky bets on those rare companies that will actually convert cutting-edge research into commercially successful products.

Or does it? Brian Lim, founder and CEO of Santa Barbara, CA-based Atomate, believes he has found a unique way of capitalizing on the latest gold rush, nanotechnology. Rather than attempting to develop specific nanotech products, such as nanowires or nanomachines, Lim and his colleagues are selling fabrication systems to other nanotech researchers. "We're selling the pans to the prospectors," he says—not trying to do the prospecting.

Atomate's "pans" are a bit more sophisticated than those of yore. Fabricating nanotech devices is intrinsically difficult and requires specialized machinery. "Nanotech researchers have been purchasing equipment designed to fabricate microchips on silicon and then customizing it for nanotechnology," Lim explains. He and his team, which includes several experienced nanotechnologists, realized that they could provide a tremendous boost to researchers, many of whom operate on constrained university budgets, by producing equipment that's already adapted for the nano world.

SCORECARD: ATOMATE

ELEVATOR PITCH	Fabrication technology for nanotechnologists
FUTURE VISION	Atomate's systems will power mainstream nanotech production
CEO'S INSOMNIA	Nanotech won't make it out of the laboratory
LEG UP	Strong industry experience coupled with in-demand products

According to Lim, a researcher might spend $100,000 or more on a silicon fabrication machine and then invest another $50,000, plus several valuable months, modifying it before he or she could carry out any nanotech experiments. Instead, the researcher can purchase a ready-built system from Atomate and be up and running much more quickly for "about the price of a Volvo."

Of course, the rapid evolution of nanotechnology requires the continual development and adaptation of fabrication systems as new processes are created, but Lim believes his products give customers a huge head start. Indeed, some customers are now coming back to Atomate with requests for specific modifications to their systems—another source of revenue for Atomate. These customers have decided that Atomate is best suited to manipulating the fabrication machinery, thus freeing their own researchers' time and attention for actual experiments.

While Lim must protect his clients' jealously guarded intellectual-property secrets, he believes that Atomate's role as the industry's "pan" provider enables him to accurately predict where nanotech is going and what fabrication machinery it will require. Like everyone in the industry, Lim awaits the breakthrough that will move nanotech from the research lab to the factory. When it appears, he plans to shift Atomate's focus from low-cost research systems to full-scale factory fabricators.

Toward that end, Lim has been patenting fabrication techniques and processes he believes are critical to the future large-scale manufacturing of nanotech products and is weighing plans for expanding the company. Lim founded Atomate just 18 months ago with an angel investment of about $1 million; nonetheless, he says it is close to breaking even and doesn't necessarily need further investment. Still, he would love to hire more researchers to continue to develop and patent techniques.

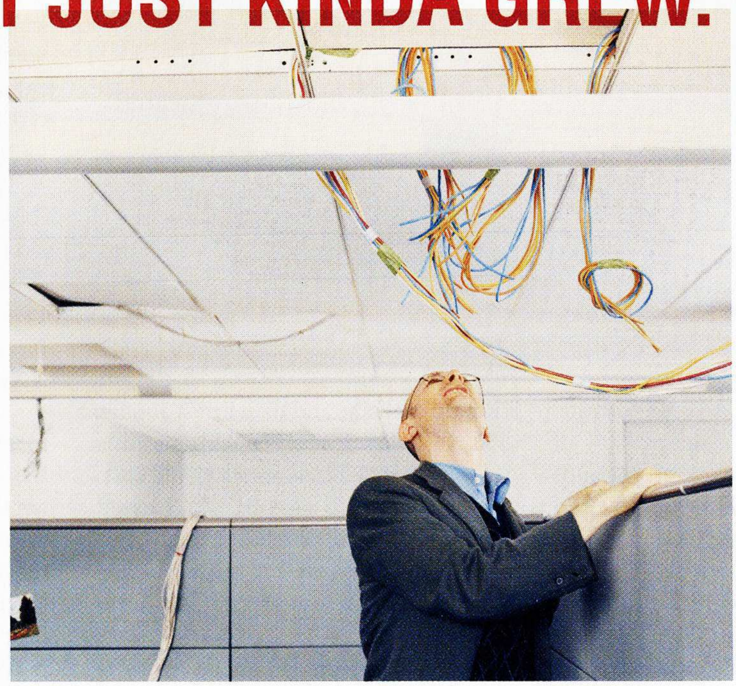
Whether to grow organically and profitably as revenues increase from the existing customer base or bring in additional investment and ramp up operations (unprofitably) in anticipation of a major industry breakthrough is a critical decision for Lim and his team. Organic growth is the safe but slow path—one that may allow competitors to leap past Atomate.

Oddly enough, a load of new investment can *raise* the risk of failure. Cash in the bank guarantees short-term survival, but the corresponding increase in expenses creates a widening hole that can only be filled by an increase in revenue. Startups survive on a diet of optimism and improving prospects, with key employees accepting pay cuts in exchange for stock options and hope. Once new people are hired, salaries raised, and office space occupied, it's hard to scale back without disillusioning employees and investors alike.

Of course, the road to success rarely rises straight up, and everyone has to be prepared, at least mentally, for things not to go precisely as planned. In technology startups, as in any form of prospecting, it's good to be good, better to be lucky, but best to be both. TR

Joe Chung cofounded Cambridge, MA-based Art Technology Group. Neither he nor *TR* holds any financial interest in the companies profiled nor endorses them as investments. To share your company's story with Joe, e-mail joe.chung@technologyreview.com.

"WE DIDN'T BUILD THIS
I.T. SYSTEM.
IT JUST KINDA GREW."



SIR TIM BERNERS-LEE

HE CREATED THE WEB. NOW HE'S WORKING ON INTERNET 2.0.

Q&A BY MARK FRAUENFELDER PHOTOGRAPHS BY ASIA KEPKA

CREATING THE WORLD WIDE WEB didn't make Tim Berners-Lee instantly rich or famous. In part, that's because the Web sprang from relatively humble technologies. Berners-Lee's invention was based on an information retrieval program called Enquire (named after a Victorian book, *Enquire Within upon Everything*), which he wrote in 1980 as a contract programmer at the European Organization for Nuclear Research (CERN) in Geneva, Switzerland. In part, it's because Berners-Lee did the unthinkable when, more than a decade later, he finished writing the tools that defined the Web's basic structure: he gave them away, with CERN's blessing, no strings attached. While others made millions off his invention, the soft-spoken programmer went on to found the World Wide Web Consortium (W3C) at MIT, which he still directs, to promote global Web standards and development. ▪ Berners-Lee is finally getting his reward: in July he was knighted by Queen Elizabeth II, and the previous month he received Finland's million-euro Millennium Technology Prize, awarded "for outstanding technological achievements that directly promote people's quality of life, are based on humane values, and encourage sustainable economic development." ▪ Now in new offices in MIT's Frank Gehry–designed Ray and Maria Stata Center, the 49-year-old native of England is busy overseeing hundreds of projects at the W3C. He is also personally

The Web's new home: Tim Berners-Lee outside his new offices in MIT's colorful Stata Center, designed by Frank Gehry.

engaged in developing his second big idea: the Semantic Web, which adds definition tags to information in Web pages and links them in such a way that computers can discover data more efficiently and form new associations between pieces of information, in effect creating a globally distributed database. Though part of Berners-Lee's original intention for his invention, the Semantic Web has been 15 years in the making and has met its share of skepticism. But Berners-Lee believes it will soon win acceptance, enabling computers to extract *meaning* from far-flung information as easily as today's Internet simply links individual documents.

The Semantic Web, coupled with other specifications and tools being developed at W3C, including accessibility standards for disabled people and software for mobile devices, is part of Berners-Lee's grand vision of "a single Web of meaning, about everything and for everyone." But is it a tangled web we weave? Despite his excitement about the future, Berners-Lee worries that poorly conceived changes to the Web's organization and governance could compromise its inherent functionality and "universality." The father of the World Wide Web shared his concerns—and dreams—the day before flying to Helsinki to accept his Millennium prize.

TECHNOLOGY REVIEW: For several years, you've been promoting something you call the Semantic Web, but people don't seem too excited. Why not?

TIM BERNERS-LEE: It's not the first time I've had this paradigm-shift problem. Early on, people really didn't understand why the Web was interesting. They saw it in the smaller scale, and it's not interesting in the smaller scale. Same thing with the Semantic Web.

TR: How do you get past that?

B-L: Right now we are just starting by putting applications onto the Semantic Web one by one and linking them up where it seems useful. But what's exciting is the network effect. The vision is that we will get to a critical mass, where everything starts getting linked into an unimaginably large whole. Then, the incentive to add more to it rises exponentially as the value of what is out there also does.

Because few people initially get this great "aha!" of connecting to a huge mass of Semantic Web data, it all has to be done by people who are convinced—who understand that it's worth putting the effort into getting the thing off the ground.

TR: Then please explain: Why is it worth all this up-front effort?

B-L: The common thread to the Semantic Web is that there's lots of information out there—financial information, weather information, corporate information—on databases, spreadsheets, and websites that you can read but you can't manipulate. The key thing is that this data exists, but the computers don't know what it is and how it interrelates. You can't write programs to use it.

But when there's a web of interesting global semantic data, then you'll be able to combine the data you know about with other data that you don't know about. Our lives will be enriched by this data, which we didn't have access to before, and we'll be able to write programs that will actually help because they'll be able to *understand* the data out there rather than just *presenting* it to us on the screen.

TR: How does the Semantic Web understand data?

B-L: Suppose you're browsing the Web and you find a seminar advertised, and you decide to go. Now, there is all sorts of information on that page, which is accessible to you as a human being, but your computer doesn't know what it means. So you must open a new calendar entry and paste the information in there. Then get your address book and add new entries for the people involved in the seminar. And then, if you wanted to be complete, find the latitude and the longitude of the seminar, and program that into your GPS [Global Positioning System] device so you could find it.

It's very laborious to do all this by hand. What you would like to be able to do is just tell the computer, "I'm going to this seminar." If there were a Semantic Web version of the page, it would have labeled information on it that would tell the computer "this is an event," and what time and date it is. And it would automatically add your travel to your event book. It would add the people to your address book, and it would program your GPS to give you directions. It would have the relationships between the event and the various people chairing it. And *those* people would have Semantic Web personal pages, which contained information about how you could contact them.

Your address book can now grow from a closed repository of private data to a view on the people-related data in the world.

TR: Does the Semantic Web, then, merely automate many of the things that a human assistant would do?

B-L: No. A human assistant uses a form of intelligence that we are not mimicking here. The human assistant will have the human mind's ability to suddenly think of correlates across the whole spectrum of his or her experience. "I've booked you through Tiawicha because they have the flower festival that weekend, I think, and...well, maybe you'll like it" is a human thought process.

This is more like giving you a program which can do all the things which your MIS department could write programs to do but doesn't have time to. But it is still a program. Just as the World Wide Web is still a document.

In the future, the Semantic Web will be a great place to develop artificial intelligence, AI, in the strong sense. But right

A SHORT HISTORY OF THE WEB

1945
In the *Atlantic Monthly*, director of the U.S. Office of Scientific Research and Development Vannevar Bush describes the Memex, a hypothetical device for linking microfiche documents.

1968
The Stanford Research Institute's Douglas Engelbart demonstrates an "oNLine System" (NLS) whose features include hypertext browsing, editing, and e-mail. To enable it, he invents the mouse.

1980
Tim Berners-Lee, a consultant with the European center for physics research CERN, writes software that allows electronic documents to link to each other.

1990
Berners-Lee dubs his global hypertext program "WorldWideWeb."

Number of websites in existence: one.

SOURCES: W3C; NETCRAFT; MATTHEW GRAY (TIMELINE)

"WE WILL GET TO A CRITICAL MASS, WHERE EVERYTHING STARTS GETTING LINKED INTO AN UNIMAGINABLY LARGE WHOLE."

1993
Marc Andreessen releases the Mosaic Web browser, which becomes the basis for Netscape.

1994
The World Wide Web Consortium (W3C) is founded. The number of websites reaches 10,000.

Berners-Lee presents the idea for the Semantic Web.

1998
W3C releases the eXtensible Markup Language (XML) specification. It allows Web page text to be tagged with descriptive labels—critical for the Semantic Web.

2000
By year's end, 25,675,581 websites have been identified.

2004
Standards that allow computers to exchange Semantic Web information are finalized.

Berners-Lee is knighted by Queen Elizabeth II.

now we are making something quite mechanical—even if we are using bits and pieces of the machinery developed by the AI community over the years.

TR: It would seem an impossibly huge task. How does the technology work?

B-L: The Semantic Web technology tackles the problem in two stages. The more mundane is a common data format. You can take a database or a calendar or an address book or a bank statement or a weather reading—basically anything with hard data in it—and make the machine write it in the basic Semantic Web language, instead of some proprietary or application-specific format. This solves the "syntactic" problem.

It still doesn't solve the "semantic" one, though. For that, the Semantic Web first gives names to the basic concepts involved in the data: date and time, an event, a check, a transaction, temperature and pressure, and location. These are all defined just to mean whatever they mean in the system which produces the data—for example, "Transaction date as I get on a bank statement," and so on. This set of concepts is called an ontology. Then, where there are connections between ontologies, such as when the date and time on a photograph is the same concept as the time on a weather report, we write rules to take advantage of these connections. This allows one to query the Semantic Web agent for photos taken on sunny days, for example. Bit by bit, link by link, the data becomes connected, interwoven. The exciting thing is serendipitous reuse of data: one person puts data up there for one thing, and another person uses it another way.

"THE EXCITING THING IS SERENDIPITOUS REUSE OF DATA: ONE PERSON PUTS DATA UP THERE FOR ONE THING, AND ANOTHER PERSON USES IT ANOTHER WAY."

TR: You've said that "phase one" of the Semantic Web is finished. Can you explain?

B-L: The way the Semantic Web works is by defining new languages for computers to exchange information. Phase one was getting those first languages, for both syntax and semantics, to the state where they became standards supported by W3C's members. Because interoperability is the key: you can't call it a Semantic Web application if the program just sits there doing things with its own data format without being able to exchange data with other programs. Now there is this foundation, and anybody who wants to make a new application and publish data can do that, and everybody else's program will be able to read the data.

TR: What kinds of Semantic Web applications are people making for the next phase?

B-L: Exciting things are happening in the life sciences. The big challenges such as cancer, AIDS, and drug discovery for new viruses require the interplay of vast amounts of data from many fields that overlap—genomics, proteomics, epidemiology, and so on. Some of this data is public, some very proprietary to drug companies, and some very private to a patient. The Semantic Web challenge of getting interoperability across these fields is great but has huge potential benefits.

TR: But it's not just a matter of exchanging data from a multitude of fields?

B-L: No. There are also challenges around maintaining privacy and intellectual property while making effective use of the information. For example, when searching for a new drug, one might want to join epidemiological data with external factors such as weather and travel and demographics to find out how a disease is transmitted and what sorts of people are predisposed to it. One may then seek to connect it to a genetic trait and start asking what proteins are associated with that, and what they enable and block in the biology of the human cell. Subsequently, one may want to connect the chemicals involved in those pathways to symptoms of diseases, and also to possible chemicals that could be used as a drug. There's a great deal to gain, which is why a lot of people are getting very fired up about working on the life sciences with Semantic Web applications.

TR: Is there an existing application that shows how the Semantic Web can form such connections?

B-L: If you want to play with the Semantic Web, you can make a friend-of-a-friend file. In a FOAF file [the data component of a personal home page, formatted in a standardized way], you can publish stuff about yourself, your organization, your publication, places, or photographs. You can have a pointer that says "this is a photograph about me" and other data about the photograph, such as who else is in it.

To create a FOAF file, you must fill out a form, such as the one at www.ldodds.com/foaf/foaf-a-matic.html. From this information, a Semantic Web–readable text file is generated that you can add to your personal website. There are semantic websites that will pull that data up and give you things like a list of photographs linking you to somebody else. I'm three photographs from Frank Sinatra because I'm photographed with Bill Clinton who's been photographed with one of the Kennedys who's been photographed with Frank Sinatra. That's a silly application, but it really shows the power of the reuse of information.

TR: Can you describe a more serious example?

B-L: It's exciting to see industry focused on implementing these standards. Tool kits from HP and IBM, authoring applications from Adobe, smart content management solutions from Profium and Brandsoft, and search engines from Network Inference are all working to create a Semantic Web at various scales. These and other technologies are being adopted by communities that in turn revolutionize how these groups collaborate and communicate. This is what's happening in life sciences, which we spoke about earlier.

In the U.K., the Semantic Web Environmental Directory is a prototype of a new kind of directory of environmental organizations and projects. Rather than centralizing the storage, management, and ownership of the information, SWED simply harvests data and uses it to create the directory. From a social per-

"WHEN YOU CLICK ON ONE OF THE PEOPLE, IT SHOWS YOU ALL THE BOARDS THEY'RE A MEMBER OF. YOU CAN START EXPLORING THE SPHERES OF INFLUENCE IN AMERICAN CORPORATE CULTURE."

spective, there's an application nicknamed Fatcats from FoafCorp [a Semantic Web project that extends the friend-of-a-friend format to corporate entities] that allows you to pick a company, and it shows you who's on its board by displaying a graph of connected people. When you click on one of the people, it shows you all the boards they're a member of. You can start exploring the spheres of influence in American corporate culture.

The exciting thing is when you find that one of these people has a FOAF file, and you start going from corporate culture into personal culture, and then into photographs, and then into weather information, and then booking flights, and then into booking restaurants, and then into figuring out what wine to have for a meal.

TR: You often talk about the importance of "Web universality." What do you mean?

B-L: One of the fundamental properties of the Web is the fact that it is just one space, and it's a consensual space. It should be independent of the hardware you use. It should be independent of the software you use or the operating system it's running on. It should also be independent of what culture you're in, or whether you're writing a wonderful, carefully edited document, or whether you're scribbling something on the back of the proverbial envelope. And it should be independent of what language you're using, what character set, whether your letters go up and down, left to right, or right to left. Also, people should be able to access that information even if they have disabilities. At W3C we call this concept "one Web—for anyone, everywhere, on anything."

TR: And there's a threat to this universality?

B-L: There was a proposal to make a special top-level domain called ".mobi." All the websites that would work with mobile phones would be put in that area; it would be the place for Web content for mobile devices. But there should be just one URL, or Web address, for something. To segregate content into a .mobi corral is the wrong way to do it. We've got lots of standards at W3C for allowing a website to perform optimally whether you're looking at it from a cell phone or from a huge screen. But obviously, if you put a ".mobi" at the end of a domain name, then you're saying, "That's a special place for stuff you can see on your cell phone."

TR: What about other top-level domains—.biz, .info, et cetera—that have been proposed to relieve the name crunch in the .com domain?

B-L: Adding new top-level domains won't help that. What people remember is the string between "www" and ".com." So if there is a .info or a .biz after it, that would just confuse them. It means that they have to remember the whole thing instead of just the brand between the "www" and the dot.

Also, of course, you have a registration fee system for financial transactions. Small companies or individuals who have a domain may feel that, in order to avoid confusion, they have to keep buying these other ones. Just the yearly rental for a family adds quite a lot to their Internet bill.

TR: There is a power struggle between the United Nations and ICANN, the Internet Corporation for Assigned Names and Numbers, which manages how domain names and Internet addresses are issued. What's your opinion?

B-L: Some countries are concerned, rightfully, that ICANN runs under a contract with the U.S. Department of Commerce. The Internet is an international thing, and even if it may be carefully run by ICANN in the best interests of the whole world, there is a strong feeling in some countries that the fact that ICANN is funded by the U.S. government means that it is U.S. controlled, and that that is unfair.

My feeling is that this asymmetry should be removed carefully. It's important that it's seen to be fair. However, the fact is that ICANN has been set up and is running, and it should not be suddenly thrown away. Making something that represents the stakeholders in a balanced way really takes a lot of experience and constant reappraisal. Maybe ICANN should have more U.N. funding, but I don't think it should have to become overnight more like a U.N. organization.

A lot of confusion in this area is caused when people use the term "Internet governance." They start off talking about domain names, which is really a very specific area, and then end up talking about privacy, copyright, confidentiality, commercial terms, and all sorts of parts of the normal legal system. People shouldn't think ICANN runs everything that happens on the Internet. ICANN just plays a very specific role.

TR: Do you believe that the World Wide Web will be your most important contribution?

B-L: My role necessarily had to morph from lone designer through community agitator to lead architect and facilitator of consensus at W3C. But I suspect the Web will be my most important contribution—although it required being in the right place at the right time. The mistake, though, is to think that it is finished. The Semantic Web is just the application of weblike design to data; it will be many more decades before we will be able to say we have really implemented the Web idea in the full, if ever we can.

TR: Besides the Semantic Web, do you have any other dreams or wishes for the future of the Web?

B-L: Oh, lots and lots! I have always wanted the Web to be a more creative, flexible medium, with annotation systems and group editors and so on. I'm excited about the new portable devices we can use for the Web, about speech-based technology, and a lot of other things. Once you start with the basic Web idea, so much stuff becomes possible. TR

Mark Frauenfelder is based in Los Angeles. His last article for *TR* was an interview with ICANN president and CEO Paul Twomey in the March 2004 issue.

ALL HYBRIDS ARE NOT CREATED EQUAL.

HYBRID

Technology Review 100

Meet the world's top young innovators. From computing to biomedicine to nanotech, their technologies will transform our lives.

INNOVATION HAS BECOME an endeavor without borders. And nowhere is that more evident than in this year's TR100—*Technology Review*'s selection of 100 top innovators under 35—a group that demonstrates that the barriers to innovation, both geographical and disciplinary, are crumbling. The TR100 for 2004, the fourth year that *Technology Review* has named its list of innovators, hail from places as varied as Singapore, Boston, South Korea, Israel, China, and India—and many are developing technologies that defy easy classification, often fusing recent advances in computing, medicine, and nanotech. On the list, you'll find leading academic researchers, entrepreneurs, social advocates for technology, and even experts in high-tech entertainment. In short, the TR100 represent the diversity of those using technology to transform the world around us. ■ Choosing the top young innovators is a challenging job—and not something we take lightly. Beginning more than a year ago, *TR* began scouring the world for nominees. As in years past, our editors then relied heavily on an expert panel of judges *(see "TR100 Judges 2004," p. 79)* who carefully whittled down the list, initially more than 600 entries, to the very best and brightest. These are incredibly talented and hardworking people, and in the following 26 pages, you'll read about their achievements and visions. Collectively this group provides an eye-opening picture of the future of technology. On page 76, you'll also read of past TR100 members, many of whom have continued to make world-transforming contributions to technology. ■ Predicting the future of technology is notoriously difficult. But it's a sure bet that the people you'll meet in the following pages will play an important role in shaping it. **—THE EDITORS**

Com-puting

Computing is all about creating better connections—whether between tiny transistors or human beings

BY NEIL SAVAGE PHOTOGRAPH BY FREDRIK BRODEN

"ONLY CONNECT," urged E. M. Forster in his novel *Howards End*. Connections, of course, are the essence of the Internet. But those connections are still getting stronger, as is clear from looking at the work of the computing-related TR100 honorees. Some are working to improve communication between nearby computer chips or along the optical network. Others are using tiny computers to gather information about the world. Still others hope to translate the ties between machines into ties that bind people, coming up with better ways to form communities. ■ Computer chips are relentlessly getting smaller, more densely packed, and faster. But the wires that carry data from one chip to another remain relatively big and slow. "The bottleneck is now the bandwidth between parts of the system," says Sun Microsystems engineer **Robert Drost**, who has pioneered a method of chip-to-chip communication that eschews wires. When a bit flips on one chip, it causes a change in the surrounding electrical field, which can be sensed by an adjoining chip and translated into a bit flip there. This approach will be key to the performance of Sun's future supercomputers. ■ Light waves already zap data and voice traffic across the Internet and the telephone network. But try to send the data any faster and the light interacts with the glass optical fibers in ways that smear the optical pulse, lowering the rate at which bits can be transmitted. Increased data speed will be needed for applications such as remote surgical procedures, to say nothing of all the people who have not yet begun to blog. "Not everyone is using the Internet today," says **Aref Chowdhury** of Lucent Technologies' Bell Labs. "As it becomes more accessible, we will see even more

demand for bandwidth." Chowdhury's optical phase conjugator performs a nifty trick that could pack more data into fiber. Normally, as a light pulse travels through a fiber, it gets distorted, and the signal gets muddier. But the phase conjugator reverses the phase of the pulse—in effect inverting its distortion. As the pulse continues down the fiber, further distortion actually undoes the inversion, restoring the original signal.

Also driving the need for more bandwidth are new sources of data, such as networked sensors. **Sokwoo Rhee**, cofounder and chief technology officer of Millennial Net in Burlington, MA, has developed a method for linking simple wireless sensors into a self-organizing network that feeds to a central computer. Such sensor networks could track objects and people, provide environmental control in an office building, and remotely monitor everything from local humidity to the presence of chemical weapons.


TR100 COMPUTING

A world of ubiquitous interconnections can be a little frightening, so some innovators are trying to help people *dis*connect. Concerned that the spread of radio frequency identification (RFID) tags might allow the covert tracking of people and their habits, **Ari Juels** of RSA Security in Bedford, MA, has developed a blocker tag that accompanies an RFID tag to prevent unwanted reading of its unique identity codes. The RFID tag would contain one privacy bit. If this bit were turned off, any scanner could read the tag. But once it was turned on at the checkout counter, the blocker tag would confuse scanners by broadcasting all possible identity codes—spamming the scanners into uselessness.

Lest the chatter of networked appliances drown out human conversation, some of the TR100 are developing better ways for computers to help people connect with each other. **Jonathan Abrams** created Friendster so people could build networks of new friends and potential dates. The system, with more than eight million users, eases introductions and helps ensure that the people on the other side of the computer screen aren't complete strangers, because you know someone who knows them. And at Meetup.com, **Scott Heiferman** works to get people offline and into face-to-face networking. His Web-based organizing tool fueled the meteoric rise of presidential candidate Howard Dean, and more than 1.4 million members use it to meet fellow fans of everything from Harry Potter to pottery.

Nuria Oliver of Microsoft feels that as more and more computers connect to each other, they should also make better connections with their human owners. "Our overall goal is to endow computers with a perception and understanding of what is happening," she says. Combining microphones and cameras with statistically based machine learning, Oliver hopes to give computers the ability to read people's facial expressions or tones of voice and make judgments about their intentions or emotional states. Your computer might, for instance, see that you're busy and block instant-message interruptions. Oliver's techniques would also provide another way for those who can't use a keyboard—young children or the disabled—to communicate with computers.

Daniel Gruhl of IBM's Almaden Research Center also wants to endow computers with a more humanlike understanding of the world. To help make sense of the mass of online data that's accumulating, he has built WebFountain, a supercomputer-based system able to examine millions of Web pages. Applying natural-language processing, statistics, and pattern recognition, the system develops an understanding of context that a keyword-based search engine couldn't match. A bank could use WebFountain to run a background check on someone with suspicious account activity and discover, for instance, that his cousin has ties to a terrorist organization that might want to use the account to launder money. "We're just beginning now to see things you can do with this technology that are different or new," Gruhl says.

As people like this year's TR100 forge new connections, computers will become better integrated into our lives. In Forster's words (easily found on the Web), "Only connect the prose and the passion, and both will be exalted, and human love will be seen at its height. Live in fragments no longer." TR

TR100 STARTUPS IN COMPUTING

INNOVATOR	COMPANY FOUNDED/COFOUNDED	TECHNOLOGY/MILESTONE
Jonathan Abrams	Friendster (Sunnyvale, CA)	Website for building networks of friends and contacts
Guido Appenzeller	Voltage Security (Palo Alto, CA)	Easy-to-use encryption technology for communications security
Serge Belongie, Vance Bjorn	DigitalPersona (Redwood City, CA)	Fingerprint authentication for computer and network logons
David Brussin	TurnTide (Conshohocken, PA)	Anti-spam router; company purchased by Symantec
Tianqiao Chen	Shanda Interactive Entertainment (Shanghai, China)	Online multiplayer gaming network; now the largest in China
Ali Hajimiri	Axiom Microdevices (Orange, CA)	Cell-phone power amplifiers
Scott Heiferman	Meetup.com (New York, NY)	Website for arranging meetings for interest groups
Michael Helmbrecht	Iris AO (Berkeley, CA)	Tiny deformable mirrors for improved biomedical imaging
Kurt Huang	BitPass (Palo Alto, CA)	Online micropayment system
Sokwoo Rhee	Millennial Net (Cambridge, MA)	Self-organizing wireless sensor networks
Ben Trott, Mena Trott	Six Apart (San Mateo, CA)	Easy-to-use software for creating and hosting weblogs

DAVID BRUSSIN

Age: 29 | Cofounder | TurnTide

All e-mail is handled by a set of rules that determines how messages get from one point to another. David Brussin, cofounder and chief technology officer of TurnTide (recently acquired by Symantec), turned those rules against spammers by building a router that examines the content and source of messages passing through it. When Brussin's router identifies a computer that's sending spam, it reduces the number of messages that computer can send out. According to Brussin, companies using the TurnTide router see spam drop by about 90 percent.

JONATHAN ABRAMS

Age: 34

Founder and chairman, Friendster

Created the Net's top social-networking site, where eight million people communicate with friends and friends of friends. The Mountain View, CA, firm has raised $14 million in venture capital.

GUIDO APPENZELLER

Age: 33

Founder and chief technology officer, Voltage Security

Started a Palo Alto, CA, firm to commercialize an encryption technology that uses a simple ID, such as an e-mail address, to ensure secure communications.

ALYSSA APSEL

Age: 31

Assistant professor, Cornell University

Adapts optical-communications technology to build receivers, transmitters, and interconnects that speed chip-to-chip communications within computers.

ANUJ BATRA

Age: 34

Systems engineer, Texas Instruments

Leads one of the industry's top teams advancing ultrawideband wireless technology, which provides the high transmission speeds needed for streaming-media applications while consuming little power.

SERGE BELONGIE

Age: 30

Assistant professor, University of California, San Diego

Created video software to analyze lab mice for adverse reactions to trial drugs. The system is related to fingerprint-matching technology he and Vance Bjorn *(see below)* founded DigitalPersona to commercialize.

VANCE BJORN

Age: 31

Chief technology officer and cofounder, DigitalPersona

Partnered with fellow TR100 honoree Serge Belongie *(see above)* to found a Redwood City, CA, biometrics company that specializes in fingerprint recognition for computer access.

J. J. CADIZ

Age: 29

Program manager, Microsoft

Invented a better approach to alleviating information overload, using a sidebar window on computer displays to track e-mail alerts, weather reports, and other data. Look for Sideshow in future versions of Windows.

TIANQAIO CHEN

Age: 31

CEO and cofounder, Shanda Interactive Entertainment

Built his Shanghai startup into China's largest online game company by specializing in multiplayer fantasy and role-playing games that now attract millions of users. Shanda's IPO last May raised $152 million.

TR100 COMPUTING

KATE SWAN (BRUSSIN); BRIAN SMALE (FREDERICK)

ROBERT FREDERICK

Age: 31 | Senior technical manager | Amazon.com

You probably think of Amazon.com as a place to buy everything from books to kitchenware. But that's only a part of what the company aspires to be. Programmer Robert Frederick is leading Amazon's transformation into something more like the Coca-Cola of e-commerce, with its own virtual vending machines—each a gateway to Amazon's entire inventory—scattered across thousands of third-party websites. It's all part of a grand vision starring Amazon as the Web's central platform for almost any kind of online purchase. ■ Frederick got his start at the company five years ago by building Amazon Anywhere, software that prepares data from Amazon's vast product database for display on cell phones and other mobile devices. From there, it was a short conceptual step to opening up Amazon's database to any independent Web merchant or programmer with a need for product information. And the resulting tools—a set of standardized commands for interacting with Amazon's database, built around XML and other new Web standards for describing content—have allowed outsiders to soup up their businesses with a range of Amazon services. ■ More than 60,000 Web developers have signed up to use Amazon's new services, with many hoping to bring new customers to their sites—and earn a commission of up to 10 percent on every sale.

AREF CHOWDHURY

Age: 32
Member of technical staff, Lucent Technologies
Invented techniques at Bell Labs that enable higher-speed transmission of data over very long distances (up to 6,400 kilometers) within fiber-optic networks.

RAFFAELE COLOMBELLI

Age: 33
Research staff member, University of Paris-Sud
Develops new types of quantum cascade microlasers with a variety of sensing and imaging applications.

ADRIAN COLYER

Age: 33
Senior technical-staff member, IBM
Leads IBM's Winchester, England-based effort to improve software quality and cut development costs through "aspect-oriented programming," an approach that promises to simplify coding for a wide range of applications.

ROBERT DROST

Age: 34
Principal investigator, Sun Microsystems
Pioneered a wireless technology to eliminate the wired connections between closely spaced chips in computer systems. The advance, enabling a 100-fold speed gain over wired connectors, will be crucial to future Sun supercomputers.

DAN GRUHL

Age: 32
Research staff member, IBM
Serves as chief architect for IBM's WebFountain system, which identifies patterns in and extracts meaning from billions of Web pages to aid business decisions and fraud detection.

MICHAEL HELMBRECHT

Age: 34
Founder and CEO, Iris AO
Fabricates microscopic, deformable mirrors on computer chips that perform image correction for medical imaging, surveillance, and other applications.

AARON HERTZMANN

Age: 30
Assistant professor, University of Toronto
Combines machine learning and graphics to capture the motion of actors, dancers, and athletes—and to generate realistic animations for films and video games.

KURT HUANG

Age: 34
Cofounder and president, BitPass
Launched a startup developing micropayments technology that allows artists, small businesses, and others to charge fees of as little as one cent for access to online content.

ARI JUELS

Age: 34
Principal research scientist, RSA Security
Devised techniques at Bedford, MA, firm to improve the security and privacy of radio frequency identification tags, as well as cryptographic tools for authentication systems based on personal information and biometrics.

RICHARD KENT

Age: 34
Assistant professor, University of Virginia
Produces biomechanical data vital to the design of air bags and auto safety systems that adjust during a crash, customizing protection to such factors as the passengers' size, weight, and physical condition.

ANDRE KULZER

Age: 29
Research engineer, Bosch
Created a thermodynamic simulation that showed the feasibility of gasoline direct injection, which lowers auto fuel consumption and emissions and eliminates the electric starter.

GOLAN LEVIN

Age: 32
Assistant professor, Carnegie Mellon University
Explores the artistic implications of information technology. For *Dialtones: A Telesymphony*, the artist and engineer choreographed the ringing of audience cell phones.

MASSIMO MARCHIORI

Age: 34
Professor, University of Venice
Develops more efficient ways of identifying, finding, and retrieving information on the Web. The computer scientist also developed the World Wide Web Consortium's Internet privacy standards.

WOJCIECH MATUSIK

Age: 31
Visiting research scientist, Mitsubishi Electric
Uses sophisticated computer graphics and image-rendering techniques at Mitsubishi Electric's Cambridge, MA, lab to create 3-D television and related 3-D photo and video systems that weave together images from multiple cameras.

JAMES O'BRIEN

Age: 34
Assistant professor, University of California, Berkeley
Invented algorithms for simulating natural phenomena such as splashing water and explosions, for use in movies, video games, and advanced training simulations.

NURIA OLIVER

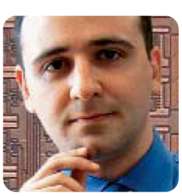
Age: 33
Researcher, Microsoft
Constructs more-intuitive human-computer interfaces. The Spanish native's projects include a smart office that can recognize what its occupants are doing and a system that lets users interact with computers via hand gestures.

RAMESH RASKAR

Age: 34
Visiting research scientist, Mitsubishi Electric
Built large computer display systems that seamlessly combine images from multiple projectors. The computer scientist's image-processing and graphics research may lead to new applications in entertainment, image-guided surgery, and user interfaces.

ALI HAJIMIRI

Age: 32 | Cofounder | Axiom Microdevices



By squeezing an entire radar system onto a single chip, Ali Hajimiri may have brought us closer to the day when even a low-end car can "see" through fog. Earlier, the Caltech electrical-engineering professor found a way to fabricate a multiwatt amplifier on inexpensive silicon with no external components—a development that could result in smaller, cheaper, less power-hungry single-chip cell phones and led him to start Axiom Microdevices of Orange, CA.

JOSHUA PAUL (HEIFERMAN)

SCOTT HEIFERMAN

Age: 32 | Cofounder and CEO | Meetup.com

In the wake of September 11, Scott Heiferman felt the need to find new ways to build community. He knew that Americans no longer belonged to bowling leagues and Elks Clubs in the numbers that they once had, but he didn't feel that electronic chat rooms and Internet personal ads filled the void. "People still live in the real world, the real non-cyber world, where they want to be face to face," he says. "The idea was, How do you use the Internet to get people off the Internet?"

So in early 2002, he assembled a five-person team to build a database and develop software that would help people organize themselves. People sign up at the Meetup.com site, indicating where they live and what topics they're interested in, and when a certain number of like-minded people in the same area have registered, the site announces a meeting. About 190,000 supporters of Howard Dean's presidential campaign used Meetup.com to organize in the months before the Iowa caucuses, giving his campaign early momentum. About 170,000 people are now registered for meetings of Democracy for America, an organization that grew out of Dean's campaign. Today, Meetup.com has more than 1.4 million registered users, and revenues at the privately funded company are seven times what they were a year ago.

Heiferman can get passionate about his theme of bringing people together, invoking de Tocqueville on the importance to Americans of forming associations and even citing an evolutionary imperative. "We're a species who was optimized for face-to-face interaction," he says. Meetup's innovations, he adds, are "as much in social engineering as software engineering."

Heiferman has been an entrepreneur since about age nine, when he founded Scott's Slave Service to market menial tasks to his siblings. And his sense of community engagement began to blossom the next year, when he wrote what he calls a "pointless letter to every U.S. governor, major-city mayor, and Fortune 100 CEO."

"The best of the Web is when there are platforms for people to do their own thing and take it in ways that the founders could never think of," says Heiferman. "What's really interesting is when the technology is merely a tool for people to do things that are uniquely human."

MARIA PETRUCCI-SAMIJA

Age: 33 | Photonics R&D program leader | DuPont

The Internet would be even faster and cheaper if more components of the fiber-optic network could be combined on individual chips—in much the way that computers evolved from room-sized monstrosities to desktop machines when transistors were condensed onto integrated circuits. Chemist Maria Petrucci-Samija has created materials that might soon make such integrated photonic circuits possible. ■ The problem with putting multiple optical components on a single chip is that different components work best when built from different, often incompatible materials. Silica glass is great for shunting a beam of light from one place to another, but it's not so good at modulating a signal so that it carries information. Petrucci-Samija has shown that plastics can be molecularly tailored to combine the best of all worlds. "It's really trying to figure out at the atomic level what is necessary to do that," she says. ■ Petrucci-Samija figured it out well enough to produce a polymer as transparent as the best optical glass; this helped the company she worked for, Lumenon Innovative Lightwave Technology, create the first polymer versions of several optical-communications components. Petrucci-Samija's work continues at DuPont, where she heads a team striving to develop new plastics and to combine plastic and silica glass devices on individual chips. She hopes to have marketable components ready for use in optical networks in about three years. ■ Petrucci-Samija says the first use of integrated photonic circuits will most likely be to make network communications more reliable and bring down the cost of equipment. Eventually, though, the same approach could help realize the dream of superfast optical computers.

JENNIFER REXFORD
Age: 34
Senior technical consultant, AT&T
Created tools for monitoring and automatically managing Internet traffic on large networks. The computer scientist's innovations are used in several systems, including AT&T's commercial backbone network.

SOKWOO RHEE
Age: 34
Founder and chief technology officer, Millennial Net
Designed extremely-low-power wireless-sensor networks at Burlington, MA, startup. The company's dime-sized sensor nodes can be used for environmental monitoring, surveillance, and health-care applications where inexpensive, long-term data collection and control are key.

SHAD ROUNDY
Age: 33
Lecturer, Australian National University
Built tiny generators for wireless sensor networks that convert low-level background vibrations into electricity, eliminating the need for batteries.

JESSE SCHELL
Age: 34
Professor, Carnegie Mellon University
Invents new forms of digital visualization. The professor of entertainment technology teaches game design and heads simulation projects, including one that helps firefighters deal with terrorism.

KEES SCHEP
Age: 34
Department head, Philips Electronics
Helped develop blue-laser optical-disc storage systems with much greater capacity than today's DVDs. The discs are now being introduced commercially.

TR100 COMPUTING

KATE SWAN (PETRUCCI-SAMIJA); EMILY NATHAN (TROTT)

CHAITALI SENGUPTA
Age: 34
Systems architect, Texas Instruments
Oversees the architecture of the communications chips used in advanced cellular systems now coming to market. The chips let multimedia cell phones more easily handle Internet access, videoconferencing, and mobile commerce.

PIERRE SILLARD
Age: 34
R&D project manager, Alcatel
Devised a software modeling tool that enabled him to design complex optical fibers now being manufactured for use in very-high-capacity communications systems.

SIMEON SIMEONOV
Age: 31
Principal, Polaris Venture Partners
Left software engineering to engineer startups. The venture capitalist advises Archivas, which uses distributed computing to manage digital archives, and Service Integrity, a Web services firm.

CHARLOTTE SKOURUP
Age: 34
Senior principal scientist, ABB
Employed "augmented reality" technologies—such as goggles that overlay the visual field with computer graphics—to help human operators program robots for industrial painting and other manufacturing tasks.

BEN TROTT
Age: 27
Cofounder and chief technology officer, Six Apart
Teamed with wife Mena *(see profile, this page)* to found the San Mateo, CA-based company that developed Movable Type, a popular and easy-to-use program for creating weblogs, and TypePad, a service that publishes them.

SRINIDHI VARADARAJAN
Age: 31
Director, Terascale Computing Facility, Virginia Polytechnic Institute and State University
Conceived and built the world's third-fastest supercomputer from a cluster of 1,100 Apple Macintoshes for $5 million. Other world-class supercomputers, in government, universities, and industry, cost $100 million or more.

MENA TROTT
Age: 27 | Cofounder and CEO | Six Apart

Mena Trott, who cofounded Six Apart with husband and fellow TR100 honoree Ben Trott *(see photo)*, liked writing a weblog but not the inflexible software it required. So while Ben pounded out code, Mena developed a simpler user interface—and the Trotts created Movable Type, which allows bloggers to create links to other pages by clicking and dragging items on-screen. TypePad, a blog-hosting service based on Movable Type, has more than 50,000 paying users.

MIN WU
Age: 29
Assistant professor, University of Maryland
Devised ways to hide digital watermarks in financial statements and other electronic documents to authenticate records, prevent fraud, and deter unauthorized distribution.

QIAN ZHANG
Age: 31
Researcher, Microsoft
Improved roaming between cellular networks and created better compression and delivery technologies for wireless multimedia. Based in Microsoft's Beijing research lab, she has more than 20 patents pending.

Nano-tech+

Tools and materials from the nano world are making headway in electronics, sensors, medical devices, and diagnostics

BY CORIE LOK PHOTOGRAPH BY FREDRIK BRODEN

NANOTECH—THE SCIENCE of building and manipulating structures at the molecular level—promises fresh perspectives on and unexpected solutions to a wide range of existing problems in semiconductors, optics, sensing, and biotechnology. Many of this year's TR100 honorees, determined to make new breakthroughs, are turning to nanotechnology to gain an unprecedented level of precision, control, and flexibility in creating new materials and devices. The nanomaterials invented by this elite group promise everything from faster and smaller electronics to more effective and targeted therapies. "When you get to the nano length scales, you can get unique properties," says Yi Cui of the University of California, Berkeley. The TR100's Nanotech+ category includes a broad range of innovations and research in materials science and energy. But it is on the scale of the ultrasmall that many of this year's TR100 are making their biggest contributions. ■ Much of the action is in biomedicine. That's because nanomaterials are just the right size to interact with important biological actors, such as proteins, DNA molecules, and viruses. Applying nanotech to biomedical problems "is a natural fit," says **Darrell Irvine**, a biomedical-engineering professor at MIT. ■ Irvine is helping to build better vaccines against diseases such as malaria and cancer by designing nanoparticles of a synthetic polymer. The nanoparticles, which carry specific stimulating molecules and antigens, are taken up by immune cells, triggering an immune response. Because of their tiny size, the nanoparticles can deliver the molecules with a high level of precision to specific receptors inside cells. That means better

control of the strength and type of the resulting immune response, which should make for more effective vaccines. Irvine has recently begun working with medical researchers at Harvard University to investigate materials that could be used to deliver an HIV vaccine.

Albena Ivanisevic, a chemistry professor at Purdue University, is employing a technique called dip-pen nanolithography to help solve a central problem for tissue engineers hoping to repair damaged body parts: controlling the precise growth of cells at specific locations. Ivanisevic coats microscopic tips with cell-nourishing peptide molecules; the tips then deposit the peptides onto a surface. The ability to arrange those peptide molecules with nanoscale precision gives Ivanisevic greater control over how and where cells will grow on the surface—ultimately forming new tissue for the body.

Nanotech also opens up new possibilities for those working to more effectively exploit or manipulate light. As anyone who has ever had to change a light bulb might suspect, conventional incandescent lighting is based on a 150-year-old technology, and researchers are eagerly looking for new ways to extend the lifetimes and boost the efficiencies of light-emitting materials. One of the favorite toys of researchers in the field is quantum dots—nanoparticles of semiconductor material that give off different colors of light depending on their size. And **Vladimir Bulovic**, a professor of electrical engineering at MIT, is using these hardy, brightly colored nano dots to reinvent the light bulb. From quantum dots, Bulovic has built novel light-emitting diodes that can be incorporated into flexible materials like plastic and should last much longer than typical light bulbs. While others, including Bulovic himself, have already developed organic light-emitting diodes, Bulovic says quantum dots can extend their effective lifetime, making them more widely usable. He's hoping to produce a highly efficient and long-lasting light-emitting flexible material in the next one to two years.

Marcel Bruchez, lead product development scientist at Quantum Dot of Hayward, CA, is also enlisting the glowing nanoparticles, but for biological imaging and the development of diagnostics. Quantum dots emit light for much longer than the conventional dyes used to track activity inside living cells, and their varied colors mean that researchers can simultaneously image multiple events and gain greater insight into the inner workings of cells. For Bruchez, the benefit of working with nanomaterials is that they open up whole new ways of thinking about problems. "It gives you greater flexibility in manipulating the materials and in putting them where you want them to go," says Bruchez.

Electronics researchers pursuing ever smaller and faster circuits are also making strides with the help of nanotech. "The silicon industry is already in the nano regime," points out **Kinneret Keren**, a researcher at Stanford University. "Now they're trying more for the molecular regime." That means using molecules such as carbon nanotubes to build next-generation electrical circuits. While other researchers have already made transistors out of individual semiconducting nanotubes, Keren decided to address the process of assembling such transistors. Her trick was to attach complementary pieces of DNA to a nanotube and to a silicon wafer; because the two pieces of DNA naturally bound to each other, they did the work of bringing the nanotube and the wafer together so as to produce a transistor. While Keren's process remains a laboratory feat, it could eventually offer a new method of efficiently manufacturing tiny circuits in which each transistor is a single molecule.

While researchers like Keren recruit biomolecules to help fabricate electronics, **Mayank Bulsara** is sticking with traditional silicon—but manipulating it in new ways. Bulsara, cofounder and chief technology officer of AmberWave Systems of Salem, NH, is developing a new form of silicon that promises to make computer chips 20 percent faster while lowering power consumption by 30 to 40 percent. The key is to stretch a silicon crystal by pulling its atoms apart just a few thousandths of a nanometer—"like a rubber band," says Bulsara. This stretching alters the properties of the material so that the electrons racing through it are less likely to collide with silicon atoms, scatter, and slow down. Bulsara hopes to have chips containing the stretched silicon on the market in major quantities by the end of next year.

This year's TR100 are just beginning to demonstrate the results of nanotech's forays into exciting new territories, but taking their work out into the real world poses its own problems. "The greatest challenge is coming up with ways of producing nanomaterials over large enough areas," says Bulovic. But when that challenge is finally met, don't be surprised if the rising stars you'll read about in the next few pages were among those who helped point the way. TR

TR100 STARTUPS IN NANOTECH+

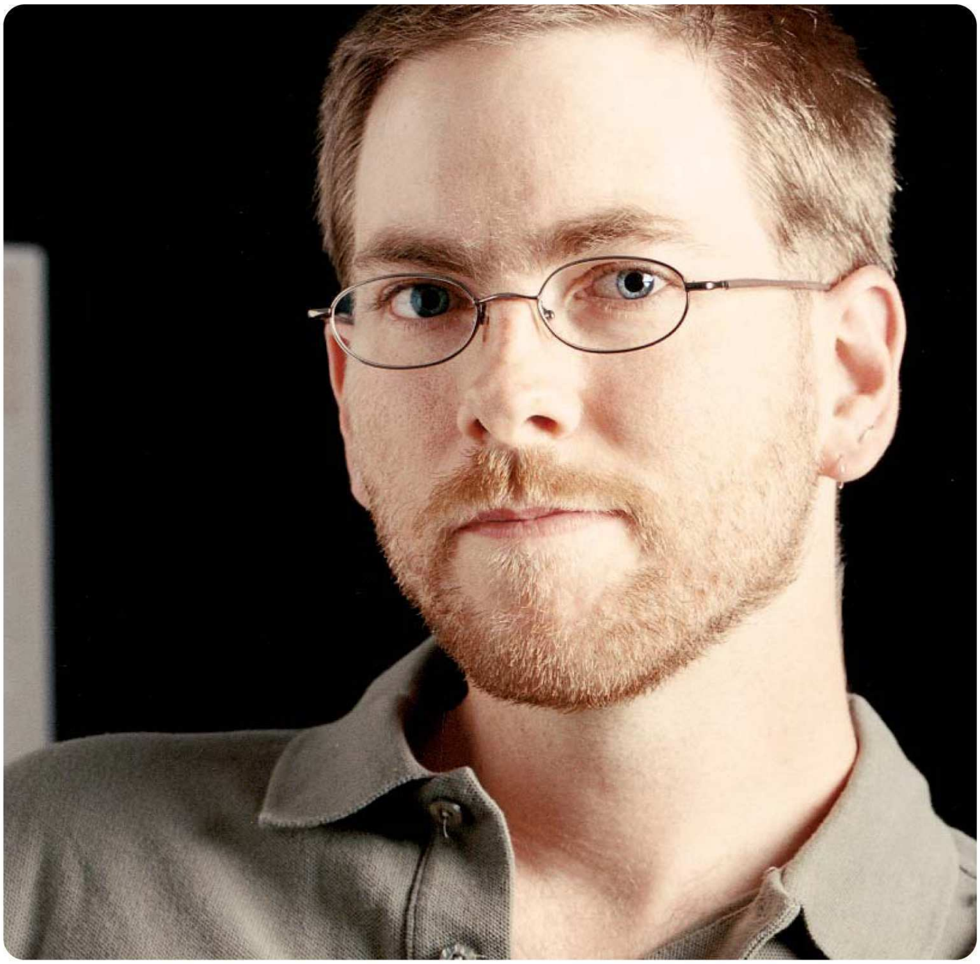
INNOVATOR	COMPANY FOUNDED/COFOUNDED	TECHNOLOGY/MILESTONES
Marcel Bruchez	Quantum Dot (Hayward, CA)	Fluorescent nanocrystals made of semiconductor material for biological labeling and diagnostics; more than 1,000 customers
Mayank Bulsara	AmberWave Systems (Salem, NH)	"Strained" silicon for faster, less power-hungry semiconductor-based devices; products containing the technology could be widely available by late 2005
Leroy Ohlsen	Neah Power Systems (Bothell, WA)	Silicon-based fuel cells for laptops and other portable electronic devices; first product could be on the market in 2006

VLADIMIR BULOVIC
Age: 34
Associate professor, MIT
Uses organic and nanostructured semiconductors in devices such as light-emitting diodes, lasers, photodetectors, and chemical sensors. Startup companies have licensed many of his 30 U.S. patents.

MAYANK BULSARA
Age: 32
Cofounder and chief technology officer, AmberWave Systems
Cofounded Salem, NH-based AmberWave to develop strained silicon, an advanced form of silicon that makes computer chips run faster and consume less power.

DUSTIN CARR
Age: 34
Principal member of technical staff, Sandia National Laboratories
Creates nanoscale silicon devices that can detect subatomic-scale movements. The nanodetectors could be used, for instance, in ultraprecise accelerometers for airplane navigation.

MARTIN CULPEPPER
Age: 32
Assistant professor, MIT
Builds the machines needed to make high-quality, low-cost nanofabrication a reality. His nanomanipulators are more flexible and offer higher performance than existing versions—at one-twentieth the cost.



MARCEL BRUCHEZ
Age: 31 | Cofounder and principal staff scientist | Quantum Dot

Six years ago, Marcel Bruchez, then a graduate student at the University of California, Berkeley, showed that quantum dots—glowing particles just nanometers wide—could be used to tag proteins inside cells. Within months, Bruchez had cofounded Quantum Dot to market the new imaging tool to biologists and drug developers seeking a more detailed picture of molecular events. It is "one of the first commercial applications of nanotechnology," says Bruchez.

LÆTITIA DELMAU
Age: 33
Research staff member, Oak Ridge National Laboratory
Helped solve fundamental problems in nuclear-waste treatment that led to an economical process for cleaning up more than 100,000 cubic meters of radioactive waste at the Savannah River Site in South Carolina, which manages the U.S. nuclear stockpile.

MARTHA GARDNER
Age: 33
Statistician, General Electric
Created statistical models and design software to make materials development more efficient. Using her methods, engineers have cut product development time by 90 percent.

VERENA GRAF
Age: 32
Engineer, DaimlerChrysler
Develops fuel cells that are practical for powering cars: they're robust, start up quickly, and have excellent power density, regardless of the weather.

YU HAN
Age: 27
Postdoctoral fellow, Institute of Bioengineering and Nanotechnology (Singapore)
Synthesized nanoscale particles with tiny, precisely defined pores. His materials can be used for the controlled delivery of drugs or for gene therapy.

PHOTOGRAPHS BY DEBRA MCCLINTON

YI CUI

Age: 28 | Research fellow | University of California, Berkeley

While some nanotech researchers create the basic building blocks of new materials, others, like Yi Cui, play equally important roles in piecing those blocks together and taking the next steps toward practical applications. Cui's ability to finely control the assembly of nano building blocks has led to new devices that may end up in cancer-screening chips, quantum computers, and solar cells.

As a chemistry PhD student at Harvard University, Cui did pioneering work on nanowires, using a combination of lasers and chemical vapors to cajole silicon to form tiny wires that not only conducted electrons but could also switch a current off and on like a transistor. Cui even fabricated nanowires whose switching depended on the presence of specific proteins, so they could serve as ultrasensitive biosensors in tests for early signs of prostate cancer.

At Berkeley, Cui has continued to master the art of building functional devices on the nanoscale. Most recently, he has found ways to precisely link together new types of nano building blocks called nanotetrapods—dots of material a few nanometers wide, each with four nanorods that radiate out in different directions. While other researchers have previously made nanotetrapods, Cui can link many of them together to create a web of circuitry and finely control their electrical properties. "We can get the nanotetrapods to self-assemble into whatever pattern we need," including arrays of transistors, says Cui. Because of their small size, these circuits could in theory be several times faster than the circuits in today's computer chips.

By arranging nanotetrapods into branching networks, Cui has transformed them from a raw ingredient into something that might be built into real devices, such as solar cells. And because the nanotetrapods are small enough to register the presence of individual electrons, they could even take advantage of the weird quantum properties of subatomic particles, forming the basis for new types of computers that will operate thousands of times faster than today's fastest machines. While that application is many years away, Cui has already demonstrated the possibility of building new structures using the basic ingredients of nanotech.

STEFAN HECHT
Age: 30
Assistant professor, Freie Universität Berlin
Devised a new class of polymer nanotubes and other molecular building blocks. These novel materials have potential applications in the fabrication of nanosized electronic devices.

DARRELL IRVINE
Age: 31
Assistant professor, MIT
Crafts nanoparticles that would release chemicals inside the body to "program" immune cells to combat viral infections like HIV, to tolerate transplants, or even to destroy malignant tumors.

RUSTEM ISMAGILOV
Age: 31
Assistant professor, University of Chicago
Develops microfluidics technologies that use tiny droplets to characterize the function and structure of proteins and to model complex biochemical processes. The microfluidic models should yield insights pertinent to drug discovery and medical-device design.

ALBENA IVANISEVIC
Age: 29
Assistant professor, Purdue University
Uses microscopic tips to deposit precise patterns of peptides directly onto tissues in the body. Her technique, which she's testing in pigs' eyes, could help treat or even cure blindness.

RAVI KANE
Age: 32
Assistant professor, Rensselaer Polytechnic Institute
Created a highly potent anthrax treatment in which each drug molecule blocks multiple toxin molecules rather than just one. He's extending the concept to anti-HIV therapies.

KINNERET KEREN
Age: 32
Postdoctoral fellow, Stanford University Medical School
Exploits biology-based self-assembly to build molecular electronics. She created a self-assembled molecular-electronic device—a carbon nanotube transistor—using a DNA template.

JAMIE LINK
Age: 26
Doctoral student, University of California, San Diego
Etched optical bar codes into micrometer-size pieces of silicon. She hopes to use the technology to detect pollutants in water or cancerous cells within the body.

YUEH-LIN (LYNN) LOO
Age: 30
Assistant professor, University of Texas at Austin
Invented nano transfer printing, an environmentally benign technique for patterning nanoscale features on organic electronics and plastic circuits. This nano patterning scheme could be used to make large-area flexible displays and cheap solar cells, and it could enable new medical therapies and diagnostics.

TYLER MCQUADE
Age: 33
Assistant professor, Cornell University
Creates catalysts to reduce the number of steps needed to synthesize drugs, diminishing environmentally hazardous by-products. He hopes one system will take the manufacture of Prozac, a top-selling anti-depressant drug, from four steps to just one.

TERI ODOM
Age: 30
Assistant professor, Northwestern University
Patterned silicon to create minuscule "beakers" that hold only zeptoliters (the silicon nanowells are only 50 nanometers across), ideal for growing individual nanoparticles of specific and uniform size. Such ultraprecision enables the tailoring of particles to specialized uses—as, for instance, ultrasensitive chemical sensors.

ERIK SCHER
Age: 28
Research and development scientist, Nanosys
Works on inorganic semiconductor nanomaterials that are helping Palo Alto, CA-based Nanosys develop cheap, flexible solar cells. Nanosys's partner, Matsushita, plans to incorporate the nano solar cells into building materials.

MICHAEL STRANO
Age: 28
Assistant professor, University of Illinois, Urbana-Champaign
Arrived at a new understanding of carbon nanotube surface chemistry that allows carbon nanotubes to be sorted according to their semiconducting, metallic, or insulating properties. This breaks the major roadblock that has prevented nanotubes' use in devices.

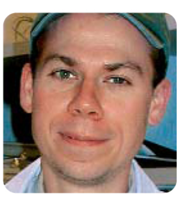
WILLIAM TAYLOR
Age: 32
Director of engineering, ArvinMeritor
Spearheads efforts to commercialize the "plasmatron," a pollution control device that converts diesel fuel to hydrogen, cutting nitrogen oxide emissions by up to 90 percent.

TSUYOSHI YAMAMOTO
Age: 31
Researcher, NEC
Demonstrated the first-ever two-qubit logic gate in a solid-state device, an advance crucial to building an ultrafast quantum computer.

SHU YANG
Age: 33
Assistant professor, University of Pennsylvania
Designs "smart" photonic devices for lightning-fast computers and communications networks. While at Bell Labs, she codeveloped a liquid microlens that can be electronically focused in milliseconds to direct light signals inside optical fibers.

YUANKAI ZHENG
Age: 34
Research scientist, Data Storage Institute (Singapore)
Simplified the production of magnetic RAM, making this fast, nonvolatile form of computer memory cheaper and more practical. A thumbnail-sized magnetic-RAM chip could store 32 gigabytes of data.

LEROY OHLSEN
Age: 30 | Founder and chief technology officer | Neah Power Systems



Fuel cells that run on methanol can power cell phones and laptops, but they're expensive and not very powerful. Leroy Ohlsen, founder of Neah Power Systems of Bothell, WA, replaced the cells' plastic membranes, which strip electrons out of the methanol to produce electricity, with porous silicon. Not only does the silicon "give us more power," says Ohlsen, but it could also cut manufacturing costs. Expect the company's first fuel cells in 2006.

STEVE DOUBLE (STEVENS)

MOLLY STEVENS

Age: 30 | Lecturer | Imperial College London

Materials scientist Molly Stevens believes that when it comes to sensing changes in the environment, nothing beats biological systems. That's why she's turning to biological molecules to create "smart" nanomaterials that could lead to new, implantable sensing and drug delivery devices. ■ Such devices would quickly detect physiological changes in the body, such as a rise in cholesterol, and respond by releasing the appropriate dose of a stored drug. That's the vision, at least. But realizing it will require new kinds of materials that behave differently under different chemical conditions. ■ Stevens has recently shown that she can control the behavior of gold nanoparticles by changing the pH of the solution in which they are suspended. She attached the particles to specially designed peptide molecules that, under the right pH conditions, interact with each other to pull the particles together into an organized structure. A change in pH alters the shape of the peptides so that they repel each other, and the particles disperse. "We're taking the best of nature's creativity and using it for ourselves," says Stevens. ■ The experiment shows that it's possible to create materials that automatically reshape themselves in response to chemical changes in the body. Such a material could yield implantable drug delivery devices that act as their own biological sensors. ■ Stevens is tapping into the versatility of peptides for the next stage of her work. She's now engineering the peptides so that they change shape in subtler and more varied ways. A drug delivery device made using such peptides would be more sensitive to physiological changes and could offer more control over a multitude of different drug dosages. If her new project succeeds, Stevens will have played an instrumental role in making not only nanomaterials but drug delivery far smarter.

Bio-tech +medicine

Researchers are tearing down the wall between the life sciences and information technology

BY ERIKA JONIETZ PHOTOGRAPH BY FREDRIK BRODEN

BIOLOGISTS AND PHYSICIANS are notorious for cyberphobia, but this year's TR100 honorees in biotechnology and medicine are erasing that stereotype—and the boundaries between the life sciences and information technology along with it. Many are pioneering fields intimately connected with or influenced by computing, areas as diverse as bioinformatics and brain-computer interfaces. Some of the most exciting advances are happening in electronic health care, synthetic biology, and ultrasensitive diagnostics. ■ With the addition of computers, "I see the whole medical process being very different—much less haphazard, much more rational," says **Colin Hill**, founder of Gene Network Sciences, which uses computer models of cells to predict how well potential drugs will work. "Ultimately, I see this future world of medicine where doctors can measure molecular activity in the body, feed it into a computer model, and determine the right treatment for the person." ■ Even before that day arrives, mobile computing will change the nature of medical practice, says **Vikram Kumar**, a resident at Boston's Brigham and Women's Hospital. He believes that simple, portable computer programs can encourage people to adhere to treatment regimens—one of the biggest challenges in medicine today. As a medical student, Kumar started a company called Dimagi to develop such tools. One example is a PDA-based game that helps diabetic kids understand how their behavior affects their blood-glucose levels. Kumar hopes that one day his management systems, combined with cheap, at-home diagnostic

tests that give patients up-to-the-minute data on their physical conditions, will keep people with chronic ailments from landing in the hospital. "The biggest dream I have is that one day we can close all the hospitals," he says.

Lauren Meyers could help him empty them out, first. By modeling how people interact in schools, hospitals, and other settings, the University of Texas at Austin mathematician can make detailed predictions about how a disease will spread. She can also use those models to determine which interventions—vaccinating health-care workers or closing schools, for example—will most effectively halt an outbreak. The British Columbia Centre for Disease Control has enlisted her help to create control strategies for future outbreaks of SARS: her models have shown that using masks in hospitals, for instance, should be as effective as more drastic measures such as closing schools.

While researchers like Meyers and Kumar are using computers in a literal sense, others are using ideas borrowed from computing to understand and even "program" living cells. In this new field of synthetic biology, "we're taking existing, well-characterized genes and putting them together in new combinations so that we get interesting behaviors," says Caltech biophysicist **Michael Elowitz**. Synthetic biologists call these new gene combinations "genetic circuits," because they provide a means of rewiring, or programming, a cell's behavior. Ultimately, these researchers hope to program cells to perform crucial tasks. Boston University bioengineer **Tim Gardner**, for instance, wants to program bacteria to develop new antibiotics, clean up the environment, or generate electricity. In each case, he's mapping the genetic pathways that control bacterial metabolism and then trying to manipulate them—to, say, turn toxins into harmless compounds.

Even in cutting-edge medical diagnostics, there are parallels to computing. Electrical engineers have found light to be the nearly perfect medium for transferring data quickly and precisely; similarly, biomedical engineers are using light to obtain information about the body on a finer scale than ever before possible—so that they can detect diseases much earlier and with greater sensitivity.

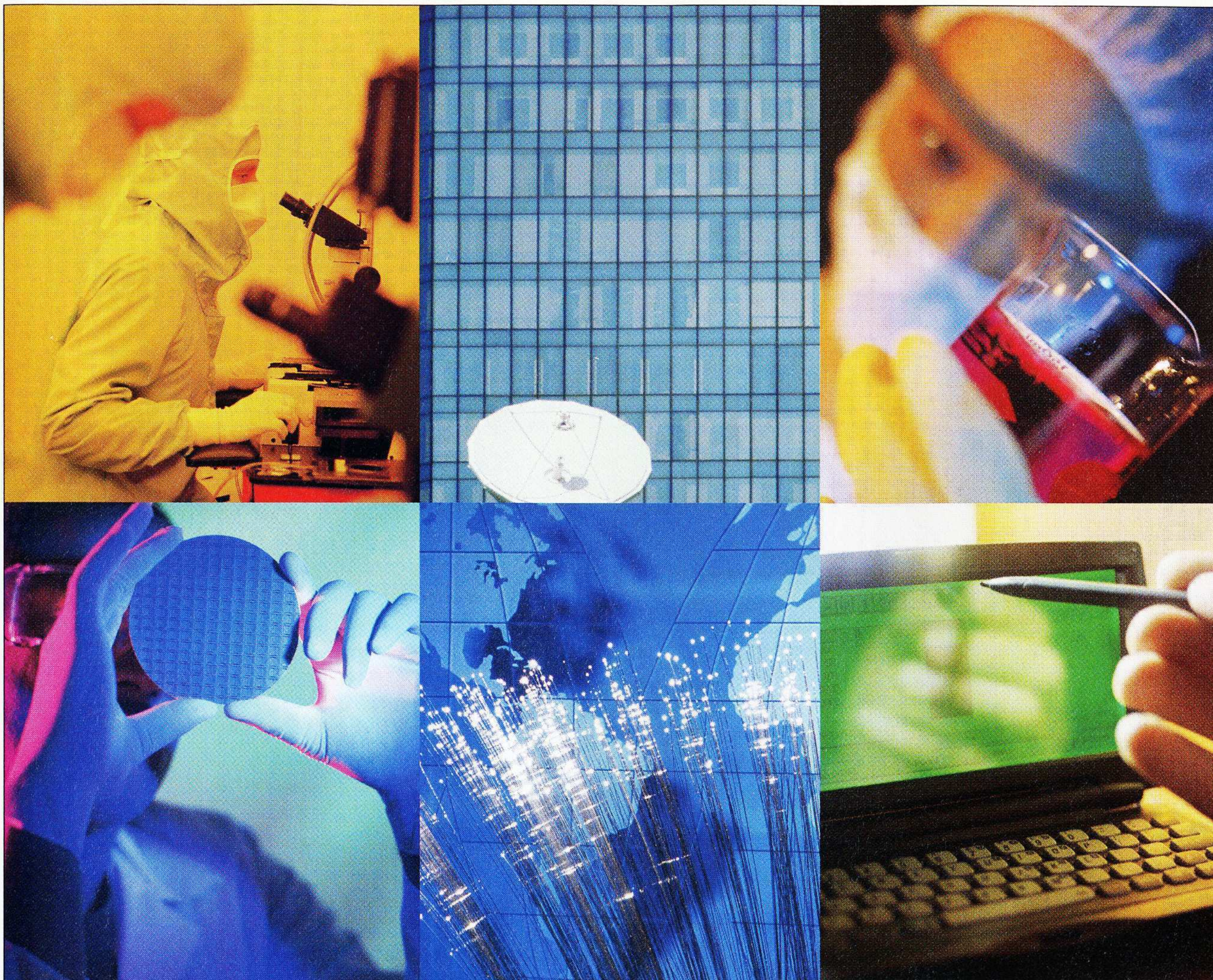
"The sooner you detect, the better," says **Vadim Backman**, a bioengineer at Northwestern University. Many cancers are curable if doctors detect them early enough, and Backman aims to make sure they do. With his technique, a doctor simply shines light on biological tissue. By collecting and analyzing data about light's wavelength, direction, and polarization as it bounces off different tissues, Backman has developed "fingerprints" of the minute structural changes in cancerous cells. This sensitivity has allowed him to detect colon cancer in rats earlier than with any other method; human tests have already begun. By inserting a probe only 1.5 millimeters wide just a few centimeters into a patient's rectum, a doctor should be able to predict whether the patient has precancers in any part of the colon. Backman hopes this will provide a cheap, quick, and easy screen for colorectal cancer.

Vasilis Ntziachristos at Harvard Medical School has similar goals. He has developed the hardware and software needed to produce 3-D images that reveal the locations of telltale molecules, such as cancer-related proteins, deep inside the body. Monitoring such molecules could allow physicians to make earlier and more precise diagnoses than they can by examining the anatomical features detected by imaging techniques such as CT and MRI scans. Today, the technology, which is similar to a CT scan but uses fluorescent tags and beams of infrared and visible light instead of radioactive dyes and x-rays, is used to observe molecules at work in living animals, helping researchers decipher how cells normally function and what goes wrong in disease. Within a few years, doctors may be able to use such molecular-imaging tools to detect tumors smaller than one millimeter in size.

These researchers don't think small, and some of their goals may take decades to reach. Yet within our lifetimes, says Kumar, electronic health care, synthetic biology, ultrasensitive diagnostics, and other technologies will combine to create a whole new way of practicing medicine, allowing doctors to personalize treatments and even prevent illnesses before they strike. Hill agrees. "It's going to be profound, more so than a lot of the discoveries that happened in the physical sciences and computing sciences," he says. "Science is finally about life now; it's finally about us." TR

TR100 STARTUPS IN BIOTECH + MEDICINE

INNOVATOR	COMPANY FOUNDED/COFOUNDED	TECHNOLOGY/MILESTONES
Ryan Egeland	Oxamer (Oxford, England)	Supercheap DNA chips for research and diagnostics; produced using proprietary electrochemistry
Tim Gardner	Cellicon Biotechnologies (Boston, MA)	Precise mapping of bacterial gene pathways to discover novel antibiotics for treating resistant infections
Colin Hill	Gene Network Sciences (Ithaca, NY)	Predictive modeling of cells to speed drug discovery; raised about $9 million
Shana Kelley	GeneOhm Sciences (San Diego, CA)	Molecular diagnostics using electrochemical detection of DNA and RNA; plans to introduce first products in 2004
Gloria Kolb	Fossa Medical (Needham, MA)	Devices to treat the urinary and biliary tracts; four have received U.S. Food and Drug Administration approval
Vikram Kumar	Dimagi (Boston, MA)	Computer tools to help patients and health-care providers; PDA tools in use in India and South Africa
David Liu	Ensemble Discovery (Cambridge, MA)	Using DNA to direct the synthesis of drugs and other chemicals; raised $15 million in its first venture round
Ananth Natarajan	Infinite Biomedical Technologies (Baltimore, MD)	Neurology, cardiology, and gynecology devices; two in clinical trials; raised $9.5 million in government funding
Sandra Waugh Ruggles	Catalyst BioSciences (South San Francisco, CA)	Designing protein-cutting enzymes to treat cancer and inflammation; recently closed first venture round



YAAKOV BENENSON

Age: 28 | Graduate student | Weizmann Institute of Science

Yaakov Benenson wants to shrink your doctor. Or more accurately, he wants to replace physicians with molecular machines that diagnose and treat diseases with phenomenal precision, each what he calls a "doctor in a cell." ■ In just five years, Benenson has taken the concept from drawing board to test-tube prototype. Working at the Weizmann Institute of Science in Rehovot, Israel, he has built molecular devices—essentially DNA strands and enzymes—able to analyze genetic changes associated with lung and prostate cancers and to release a drug in response. These prototypes are "a beautiful work of molecular and conceptual integration, pointing the way toward truly integrating diagnostics with therapeutics," says George Church, director of the Center for Computational Genetics at Harvard Medical School. ■ "Using these tiny diagnostic machines, we could selectively treat only the diseased cells," Benenson says. For example, the prototype device for small-cell lung cancer assesses the activity of four genes. Cancerous cells produce extra RNA copies of each of these genes. Consecutive sections of the DNA strand in the prototype bind, in turn, to these RNA strands; when they do, an enzyme chops them off. If all of the cuts are made properly, the enzyme releases and activates an anticancer drug that has been tethered to the DNA in an inactive form. ■ Benenson's molecular machines offer a unique combination of precision and flexibility. A single one of them can be designed to look for up to 10 different diagnostic markers before it releases its drug payload. The devices can also be tailored to several different diseases through simple-to-make changes in their DNA sequences. ■ These machines represent a quantum leap not only in medicine but also in DNA computing. Benenson's molecular "doctors"—which are computers in the sense that they store information and analyze it following a yes/no logic—are "directed at a practical interface with biomedicine rather than losing an abstract race with existing computers on their own turf," says Church. ■ It will be a while before molecular machines replace existing systems of diagnosis and treatment: Benenson estimates three or four years before even simple versions that work in a living cell are ready, and perhaps decades before they can be tried in people. If the DNA doctors prove as successful in the body as they have in the lab, though, they might spark a revolution in medicine.

VADIM BACKMAN
Age: 31
Assistant professor, Northwestern University
Found a way to spot colon cancer earlier than was previously possible—and well before it has spread—by measuring the changes that occur when white light interacts with tumor cells.

SELENA CHAN
Age: 31
Research scientist, Intel
Designs nanotechnological tools to detect viruses, bacteria, and, for the first time, single molecules of DNA in medical samples.

REBEKAH DREZEK
Age: 30
Assistant professor, Rice University
Develops photonic technologies that use targeted nanomaterials to detect, monitor, and treat breast and gynecologic cancers painlessly, and at a fraction of the cost of conventional approaches.

RYAN EGELAND
Age: 29
Director and cofounder, Oxamer
Slashed the cost of producing a DNA chip from hundreds of dollars to a few dollars by combining microfluidics, computer control, and novel electrochemistry. Cofounded Oxford, England's Oxamer with genetic-analysis pioneer Edwin M. Southern to commercialize the technology.

MICHAEL ELOWITZ
Age: 34
Assistant professor, Caltech
Combines existing genes to build artificial biological pathways, or "circuits," that operate inside cells. The goal: better understanding how cellular behavior is naturally controlled—and how it might be reprogrammed.

TIM GARDNER
Age: 31
Assistant professor, Boston University
Constructs computer models of cellular pathways in order to optimize bacteria for energy production and environmental remediation. Cofounded Cellicon Biotechnologies in Boston, MA; the company uses the cellular models to improve antibiotics.

SHANA KELLEY
Age: 34
Assistant professor, Boston College
Builds nanoscale electrochemical and electrical sensors to detect medically relevant gene sequences and proteins. Cofounded San Diego, CA's GeneOhm Sciences to produce molecular diagnostics based on one such technology.

GLORIA KOLB
Age: 32
Founder and president, Fossa Medical
Devised a way to remove kidney stones more cost effectively and less invasively by taking advantage of the ureter's tendency to dilate around foreign objects. Her Boston-based company has two devices on the market.

VIKRAM SHEEL KUMAR
Age: 28
Cofounder and CEO, Dimagi
Founded Dimagi in Boston to develop interactive software that motivates patients to manage chronic diseases such as diabetes and AIDS. His PDA-based systems are being used in rural India and South Africa.

JÖRG LAHANN
Age: 33
Assistant professor, University of Michigan
Designed an electrically switchable surface coating that can alternate between attracting and repelling water. Such "smart surfaces" could coat biomedical implants for use in tissue engineering, sensing, or drug delivery.

ERIC C. LEUTHARDT
Age: 31
Resident physician, Washington University School of Medicine
Showed that a patient could achieve real-time control of a computer via electrodes placed on the brain's surface. Such an interface could allow paralyzed people to communicate and, eventually, control prostheses.

DAVID LIU
Age: 31
Associate professor, Harvard University
Applies evolutionary principles to synthetic molecules by linking starting materials to DNA strands; the strands' sequences determine which of them bind to each other, and thereby direct reactions between the starting materials.

FRANK LYKO
Age: 34
Group leader, German Cancer Research Center
Aims to reprogram cancer cells to be more like normal cells by developing compounds that block the aberrant modification of DNA in cancer cells.

LAUREN MEYERS
Age: 31
Assistant professor, University of Texas at Austin
Helped public-health officials control epidemics of walking pneumonia and SARS with sophisticated mathematical models that predict how a disease will spread through networks of human interactions.

ANANTH NATARAJAN
Age: 33
CEO, Infinite Biomedical Technologies
Cofounded his Baltimore, MD, firm to bridge the gap between research and patient care. One of its technologies will enable implantable cardiac devices to detect incipient heart attacks.

VASILIS NTZIACHRISTOS
Age: 34
Assistant professor, Harvard University
Facilitated noninvasive optical imaging of proteins and other molecules in the body—which could lead to ultraprecise diagnosis of cancer and other diseases—through his theories, software, and instruments.

SHAYN PEIRCE
Age: 29
Assistant professor, University of Virginia
Models how individual cells in tissues migrate, multiply, and develop during processes such as blood vessel growth. The models should aid tissue engineering and drug development.

COLIN HILL
Age: 32 | Cofounder and CEO | Gene Network Sciences

Four out of five drugs fail in human trials. But Colin Hill says that at his Ithaca, NY, startup, "We think we are the answer." The physicist turned entrepreneur aims to more than double human trials' success rate by virtually prescreening drugs in computer models of human cells. His company uses these "virtual cells" to uncover how the compounds work and predict which ones will fare best in human tests. Drugmakers share his enthusiasm: his company has deals with two of the top five drug firms.

NATAN DVIR/GETTY IMAGES (BENENSON)

SANDRA WAUGH RUGGLES
Age: 30
Cofounder and scientist, Catalyst Biosciences
Uses clever testing schemes to determine which protein-slicing enzymes make the cut as potential drugs. Her South San Francisco company is developing the protease-based treatments for cancer and inflammation.

CHRISTOPH SCHAFFRATH
Age: 33
Business development manager, Onyx Scientific
Discovered, as a grad student, an enzyme that could enable environmentally benign production of fluorine-containing compounds such as Teflon and Prozac, which are now made via noxious chemical processes.

MONISHA SCOTT
Age: 33
Director, Target Discovery and Validation, Inimex Pharmaceuticals
Determined how small, natural proteins boost the immune response. Inimex, in Vancouver, British Columbia, develops synthetic versions of the proteins for antibiotic-resistant infections.

CHRISTINA SMOLKE
Age: 29
Assistant professor, Caltech
Fine-tunes the activity of individual genes via an adaptable technology that is potentially useful in biosensors, gene therapies targeted to specific types of cells, and the development of new antibacterial, antifungal, and anticancer treatments.

SMRUTI VIDWANS

Age: 30 | Postdoctoral fellow | University of California, San Francisco

Tuberculosis kills two million people every year, a tragedy of which Smruti Vidwans was all too aware growing up in India. Resistance to TB drugs is on the rise, and Vidwans thinks the solution may be new drugs that don't kill the bacteria but block the proteins that allow them to reproduce in people. She's launching a company to develop such drugs. It's a huge challenge, but those who know her say she's up to the task.

KAHP-YANG SUH
Age: 32
Assistant professor, Seoul National University
Came up with the first method that allows researchers to pattern proteins and cells directly onto glass or plastic surfaces or within microfluidic channels without complicated preparation. The technique is potentially a boon not only for basic research but also for the development of chemical and biological sensors.

OLGA TROYANSKAYA
Age: 26
Assistant professor, Princeton University
Devised sophisticated and accurate computer algorithms for analyzing data generated using DNA microarrays. These algorithms allowed her to identify genes involved in a host of diseases, including lymphoma, lung cancer, and gastric cancer.

LEI WANG
Age: 31
Research fellow, University of California, San Diego
Expanded the genetic code in order to allow living cells to incorporate new, unnatural building blocks into the proteins that they make. The technique could one day allow biologists to create new proteins and even entire organisms that have enhanced or novel properties.

EMILY NATHAN (VIDWANS); ASIA KEPKA (ZHUANG)

XIAOWEI ZHUANG

Age: 32 | Assistant professor | Harvard University

Xiaowei Zhuang makes movies of the invisible. Peering into a microscope, she has filmed a single influenza virus infecting a cell. Her studies mark the first time anyone has recorded the stages of this process. ▪ Zhuang accomplished this feat by attaching fluorescent molecular tags to the virus; when excited with a laser, the tags emit specific colors of light. She has used the approach to track the behavior of not only individual viruses but even individual molecules, such as strands of RNA, at unprecedented levels of detail. Coming from a traditional physics PhD program, Zhuang very quickly began to lead experiments in single-molecule biophysics as a postdoc in Steven Chu's lab at Stanford University. "With total ease, she immersed herself in biological physics and did an astounding amount of seminal work," Chu says. Since establishing her own lab at Harvard, Zhuang has continued to do "landmark experiments at a blistering pace," he adds. ▪ Direct observations of individual molecules are essential to really understanding how life works, Zhuang believes. "In the biology world, there are a lot of very small things that are doing critical functions," she says. "There is a lot of interesting dynamic information one can get out of this kind of single-particle approach." In her work on the flu virus, for example, Zhuang discovered that viruses move through the cell in three stages—one of which is so short that it could only be directly observed with high-speed imaging. "This experiment revealed unprecedented details of virus infection pathways," says Harvard chemist Sunney Xie. ▪ Eventually, this in-depth understanding of how viruses work will help researchers find entirely new ways of blocking viral infection, Zhuang says. Indeed, virologists have begun asking to work with Zhuang, hoping to use her methods to study their own pet viruses.

Where Are They Now?

BY BRAD STENGER

A VIRUS THAT KILLS HIV, a 3-D display for airport scanners, God's own guitar distortion pedal, and a public-health analogy to the Internet. It can only mean one thing: former TR100 honorees are still at it, solving problems with creativity, innovation, and fortitude.

FIGHTING DISEASE

University of Oxford biochemist **Ben Davis** (2003) discovered a new class of compounds he's calling glycodendriproteins that act as front-line fighters against infectious disease. The compounds bind to bacteria and prevent them from gaining the foothold in human tissue they need to reproduce. Unlike antibiotics, Davis's compounds reduce the risk of superbugs that evolve drug resistance, as some forms of tuberculosis and staph infection already have. New technologies are making it possible to find better ways to fight disease, says Davis. "My grandma is 94. She lived through the era when antibiotics were discovered and then dominated. It's time to find something new."

David Schaffer (2002) and **Adam Arkin** (1999), colleagues at the University of California, Berkeley, gained attention for their unique proposal for fighting AIDS. Using computer models developed by Arkin, Schaffer and grad student Leor Weinberger engineered a living virus that can attach itself to HIV and kill it. Trading a deadly virus (HIV) for a seemingly benign one (Schaffer's) could have unforeseen consequences. However, says Schaffer, "Society might one day think...creating parasites to fight parasites is worth the risk." There's plenty of time to weigh possibilities, though, as clinical trials are still years away.

Until researchers can shut down diseases entirely, **Paul Meyer** (2003 Humanitarian Award) and his Washington, DC-based company Voxiva are working to ensure that outbreaks don't become epidemics. The company develops phone- and Web-based disease surveillance systems, and since the start of 2004, it has launched projects in Washington, DC, Rwanda, India, and Nigeria. Voxiva works with government officials and local health monitors who use touch-tone phones or the Internet to report the number of sick in their areas and the severity of their illnesses. The technology has proven effective in economically or geographically isolated regions and can be targeted toward specific diseases, including HIV/AIDS and Japanese encephalitis. In the United States, public schools use Voxiva's system to report absenteeism, a possible early indicator of an outbreak.

In June, Athersys, a Cleveland company founded by **John Harrington** (2002), inked a partnership with the Juvenile Diabetes Research Foundation to find new ways to treat diabetes. The partners seek to understand how Athersys's novel adult-derived-stem-cell therapy might induce a person's pancreas to form the insulin-producing cells central to treating type 1 diabetes. Other alliances with the Cleveland Clinic and the National Institutes of Health will focus on heart and cardiovascular disease, respectively. Harrington also says that the company expects to submit drugs to treat asthma and obesity to the U.S. Food and Drug Administration in 2005 and begin clinical trials soon thereafter.

University of Chicago chemist **Milan Mrksich** (2002) developed a fast and highly accurate test for screening molecular compounds, which could aid bioterror defense and speed drug development. The test's precision comes from using mass spectrometry, well known for accurately identifying chemical composition. Its speed comes from an innovative sample preparation technique that enables Mrksich to screen 10,000 molecules in only three days; with automation, that rate could reach 50,000 molecules a day. In initial tests, Mrksich found a compound that inhibited a lethal protein on the surface of the anthrax bacterium. He is now working to better understand its structure and activity in order to develop an anthrax inhibitor.

TO MARKET

Gregg Favalora (1999), founder, acting CEO, and chief technology officer of Burlington, MA-based Actuality Systems, will not be distracted. His company recently demonstrated its walk-around 3-D displays to airport scanner manufacturers, who are eyeing better technologies to prevent terrorism. By simply walking around Actuality's 51-centimeter-diameter, glass-covered orb, inspectors can view scanned objects from all angles. Homeland security is one of a handful of markets Favalora is targeting; others include medical imaging and oil exploration. But the 30-year-old CEO doesn't want to get ahead of himself. "We're turning away customers at this point," he says. "We want to build a very large company, and we have to focus." Investors and customers like the focus. Actuality has installed 18 of its displays for clients since 2001.

American Superconductor of Westborough, MA, received a grant to develop superconducting wire for the U.S. Department of Defense. Based on technology invented by **Amit Goyal** (1999) of Tennessee's Oak Ridge National Lab, the wire transmits electrical current without resistance when cooled to the temperature of liquid nitrogen (-196 °C). Though difficult to engineer, cables made of the wire could carry three to five times as much current as copper transmission cables the same size. And while copper wire cables typically lose 7 to 10 percent of the electrical power they carry during transmission, superconductor cables lose insignificant amounts. The technology is perfect for high-energy motors in large vehicles such as ships and submarines, and for niche medical and high-energy-physics applications. But the wires will be most useful, according to Goyal, in metropolitan areas, where they will replace kilometers of under-

ground transmission wires made of copper, bringing more efficiency and power to the electrical grid. American Superconductor is scaling up a pilot manufacturing plant and expects to have commercial quantities of the wire available in 2007.

STARTING UP

Who better to develop software that can filter out songs being illegally transferred over file-swapping networks than Napster founder **Shawn Fanning** (2002)? Early this year, the 22-year-old announced he was launching San Francisco-based SnoCap to commercialize technology that creates audio fingerprints of digital songs, saves them in a database, and then looks for the fingerprints when songs are transferred to determine whether they're being used legally. Recording companies support Fanning's work, as it helps them in court battles against peer-to-peer Napster descendants like Kazaa and eDonkey.

Justin Frankel (2002) left America Online early in 2004 and started Cockos in San Francisco, where he's developing the JesuSonic, a computerized guitar distortion pedal. Right now, it's not much to look at: a circuit board inside a cardboard box, with cables running to a computer keyboard, a tiny display, and a guitar pedal. The fact that it works is somewhat miraculous, says Frankel, and the psychedelic sound it creates is so otherworldly that he calls it "God's own effects processor." Because the device will be fully programmable, Frankel hopes it will inspire communities of hacker musicians. The inventor of Winamp, a hugely popular free MP3 player, Frankel has made a career of marrying his interests in music and software. "There are a lot of similarities, making music and writing code," he says. "For one, they're both nice to share." He hasn't yet formulated his business plan and doesn't know how much of his technology he'll actually give away. But his musical experiments can be heard, for free, at www.JesuSonic.com.

Lou Montulli (2002) hopes to create a different type of music startup. He has assembled a team to make a portable music player that integrates software with Net-based services. Early prototypes allow users to organize large MP3 collections into playlists that can be discussed, compared, and traded through a communitywide Web service. If the plan comes together, Montulli would like to raise money this fall. He's also finding time to consult on Chandler, the well-known open-source personal-information manager *(see "Trash Your Desktop," TR November 2003)*, and to work with the Open Voting Consortium, an open-source e-voting project. He and a group of University of Nevada students have built a prototype system that works like an ATM. After a person votes, the machine prints a paper receipt listing his or her selections. But just before the machine spits it out, an optical scanner creates an image of the receipt and saves it to memory. These digital snapshots allow election officials to double-check electronic tallies without gathering paper. With such redundant counting mechanisms, says Montulli, "every voter becomes a quality assurance tester."

NEW LAB SPACE

Two TR100 recipients have recently taken charge of Intel-sponsored lablets, small research labs located near major universities. In June 2004, **Todd Mowry** (1999) became director of Intel Research Pittsburgh, a lab consisting of 15 Intel and Carnegie Mellon University computer scientists. Mowry hopes to advance existing work on user interfaces for "computing nomads"—people who work on the same projects from different workstations in changing locations. The vision is that you would power down the computer at your office in, say, New York City, then start up your computer at home in New Jersey, picking up right where you left off. Meanwhile, **Joe Hellerstein** (1999) was named director of Intel Research Berkeley in California. His job is to muster forces to solve problems inherent to large-scale computer networks, such as security holes. The lab developed a distributed computing system that serves as the platform for Hellerstein's own project, dubbed PHI, for Public Health of the Internet. Indeed, the effort resembles a public-health initiative: researchers analyze clumps of users to understand not only how computer viruses spread but how people's behavior increases risk. Hellerstein seeks to gather this information by simultaneously querying millions of computers over the Internet. He hopes to create a visualization tool that would synthesize the resulting data, enabling researchers to see how viruses spread around the globe.

In February 2004, Silex Microsystems, where **Helene Andersson** (2003) is business manager for life sciences, opened a new 1,000-square-meter facility near Stockholm, Sweden. The plant manufactures custom microelectromechanical parts for drug delivery devices, including micropumps designed by Debiotech, a Lausanne, Switzerland, startup, and microneedles for Haifa, Israel's NanoPass Technologies. The factory can also manufacture lab-on-a-chip devices, but according to Andersson, "Europe's big pharma companies haven't begun using the chips yet." To take up any slack in its assembly lines, Silex currently produces air-bag pressure sensors and specialty chips. Meanwhile, Stockholm's Royal Institute of Technology took up the little slack in Andersson's already busy professional life, naming her an associate professor earlier this year. TR

FOR TR100 MEMBERS, THE IPO IS NOT DEAD

TR100 honorees whose companies either went or were planning to go public between July 2003 and July 2004

COMPANY	TR100 MEMBER	TITLE
Alnylam Pharmaceuticals (Cambridge, MA)	Christoph Westphal (2002)	Venture capitalist
Color Kinetics (Boston, MA)	Ihor Lys (2002)	Chief technology officer
Epigenomics (Berlin, Germany)	Alexander Olek (2002)	Chief executive officer
Google (Mountain View, CA)	Sergey Brin (2002) Larry Page (2002)	President, technology President, products
Linspire (San Diego, CA)	Michael Robertson (1999)	Chief executive officer
Momenta Pharmaceuticals (Cambridge, MA)	Christoph Westphal (2002)	Venture capitalist
Opera Software (Oslo, Norway)	Håkon Wium Lie (1999)	Chief technology officer
Seven Networks (Redwood City, CA)	Bill Nguyen (2002)	Chief executive officer

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Alexis Rockman
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Ben Saunders
Barry Schwartz
John Sculley
Eloma Simpson Barnes
Spencer Wells

TR100 HONOREES

TR100 JUDGES 2004

Howard Anderson
Senior managing director, YankeeTek Ventures

Angela Belcher
Associate professor of materials science and engineering, MIT

Gordon Bell
Senior researcher, Microsoft Media Presence Research Group

Alexis Borisy
Founder, president, and CEO, CombinatoRx

Joe Chung
Cofounder, Art Technology Group

James Collins
Professor of biomedical engineering, Boston University

Sanjay Correa
Global technology leader for energy and propulsion technologies, GE Global Research

Ernest Cravalho
Professor of mechanical engineering, MIT

Tejal Desai
Associate professor of biomedical engineering, Boston University

Richard Friend
Professor of physics, University of Cambridge

Kent Fuchs
Dean of engineering, Cornell University

Irene Greif
IBM fellow and department group manager, Collaborative User Experience, IBM

Edward Jung
Cofounder and managing director, Intellectual Ventures

Lionel Kimerling
Professor of materials science and engineering, MIT

Christina Lampe-Onnerud
Director of power technologies, Tiax

Tod Machover
Professor of music and media, MIT Media Laboratory

Chad Mirkin
Professor of chemistry, Northwestern University

Richard Mulligan
Professor of genetics and professor of pediatrics, Harvard Medical School

Nicholas Negroponte
Professor of media technology and founding chairman, MIT Media Laboratory

Stephen R. Quake
Associate professor of applied physics, California Institute of Technology

Micah Siegel
President and CEO, Concept2Company

Michael S. Tomczyk
Managing director, Emerging Technologies Management Research Program, University of Pennsylvania

Sophie V. Vandebroek
Chief engineer, Xerox

Susie Wee
Principal research scientist and R&D department manager, Hewlett-Packard Labs

Chelsea C. White III
Professor of transportation and logistics, School of Industrial and Systems Engineering, Georgia Institute of Technology

Jackie Ying
Executive director, Institute of Bioengineering and Nanotechnology, Singapore

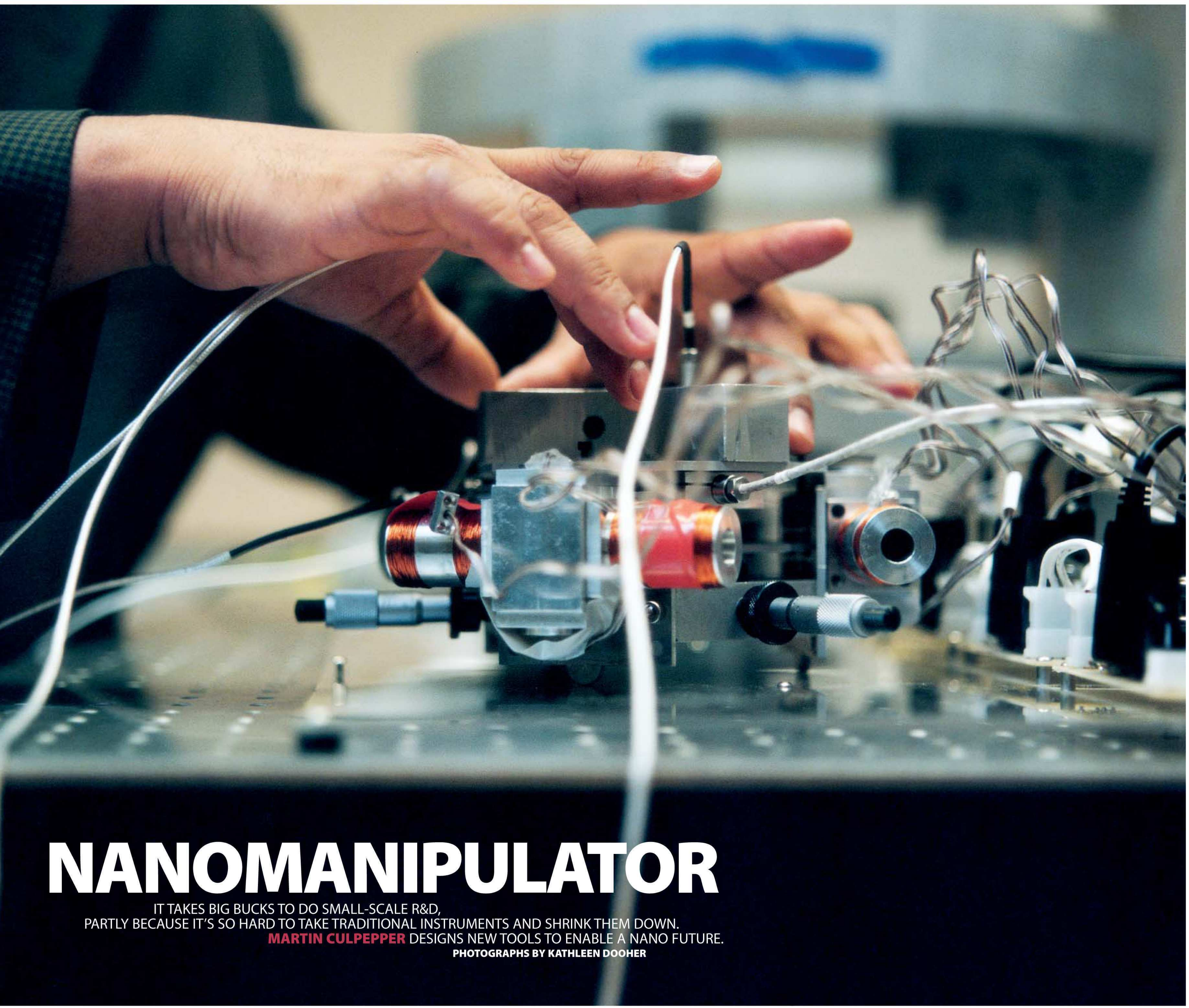
Daphne Zohar
Founder and managing general partner, PureTech Ventures

Ethan Zuckerman
Cofounder, Geekcorps

Victor Zue
Codirector of the Computer Science and Artificial Intelligence Laboratory and professor of electrical engineering and computer science, MIT

TR100 CONTRIBUTORS

Project managing editor: Bill Marbach
Assistant managing editor: Erika Jonietz
Research consultant: Brad Stenger
Fact checkers: Dan Cho, Janet Bertaud
Copy chief: Larry Hardesty
Copy editors: Thomas Motley, Kathryn O'Neill
Researchers: Janet Bertaud, Laura Levis, Luke Phelan
Writers: David Freedman, Erika Jonietz, Corie Lok, Bill Marbach, Neil Savage, Brad Stenger



NANOMANIPULATOR

IT TAKES BIG BUCKS TO DO SMALL-SCALE R&D,
PARTLY BECAUSE IT'S SO HARD TO TAKE TRADITIONAL INSTRUMENTS AND SHRINK THEM DOWN.
MARTIN CULPEPPER DESIGNS NEW TOOLS TO ENABLE A NANO FUTURE.

PHOTOGRAPHS BY KATHLEEN DOOHER

DEMO

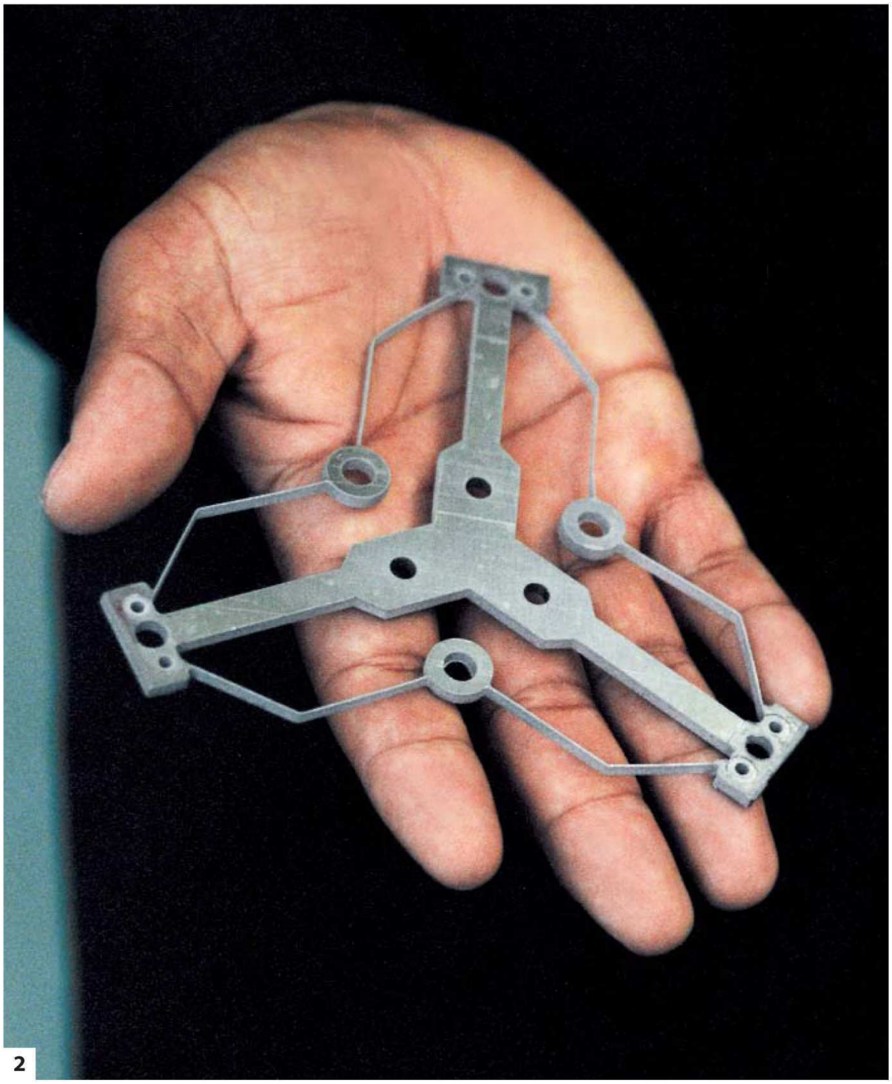
NANOTECHNOLOGISTS promise a lot: electronics forged from individual molecules, superstrong, lightweight materials, ultrafine capsules that carry drugs to specific organs or cells in the body. But to tinker with materials on that scale, researchers need tools to probe and nudge their invisibly small specimens. And manufacturers will need equipment to mass-produce these future marvels. Such instruments don't come cheap. The going price for a nanomanipulator—a machine so named not because it is tiny itself but because it can move things around with nanometer precision—is tens of thousands of dollars. MIT mechanical-engineering professor and TR100 honoree Martin Culpepper believes he can produce better instruments for less than $3,000 apiece using a different approach to machine design. Existing nanomanipulators, he points out, "have got a bunch of different joints and linkages to assemble together." Because the gaps between pieces can be many nanometers wide, this "old paradigm," as he calls it, is impractical for nanoscale motion. Instead, Culpepper's machine is built around one piece that bends and flexes ever so slightly. He shows *TR*'s Dan Cho how to provide supersmall movement without an astronomical price tag.

1

1. LIKE BUTTER. The nanomanipulator begins in a machine shop, where two of Culpepper's graduate students, Soohyung Kim and Nathan Landsiedel, cut pieces out of metal. They place a plate of titanium on the bed of a water-jet cutter and feed instructions from a computer disk into the adjoining console. With a moving nozzle that shoots a millimeter-wide stream of water laced with particles of garnet, the machine can cut complicated shapes in a matter of minutes.

2. FLEX TIME. Culpepper holds out one of the newly cut pieces. This is the heart of his machine: three flat strips branching out symmetrically from a common center and surrounded by a wiry frame to form a vague triangle. There is purpose in this curious geometry. The center, or "stage," of the triangle is where a probe would be fixed in a complete instrument. "You hold these three points," says Culpepper, gesturing toward three washer-shaped fixtures suspended on the bent arms between the corners of the triangle, then "you push each one of these tabs to the side or up and down." He indicates the ends of the flat strips and demonstrates how pushing two tabs toward each other moves the center away from them both. Press down on all three and the center moves upwards. By pushing different combinations of tabs, he can cause the stage to slide or twist in any possible direction. This is what engineers call six-axis motion, something existing nanomanipulators struggle to achieve.

3. GETTING ATTACHED. Culpepper bolts the flexible piece onto the aluminum base of his machine. A twist of one of the long knobs protruding from the sides moves the adjacent washer-shaped fixture by a few micrometers. With these knobs,



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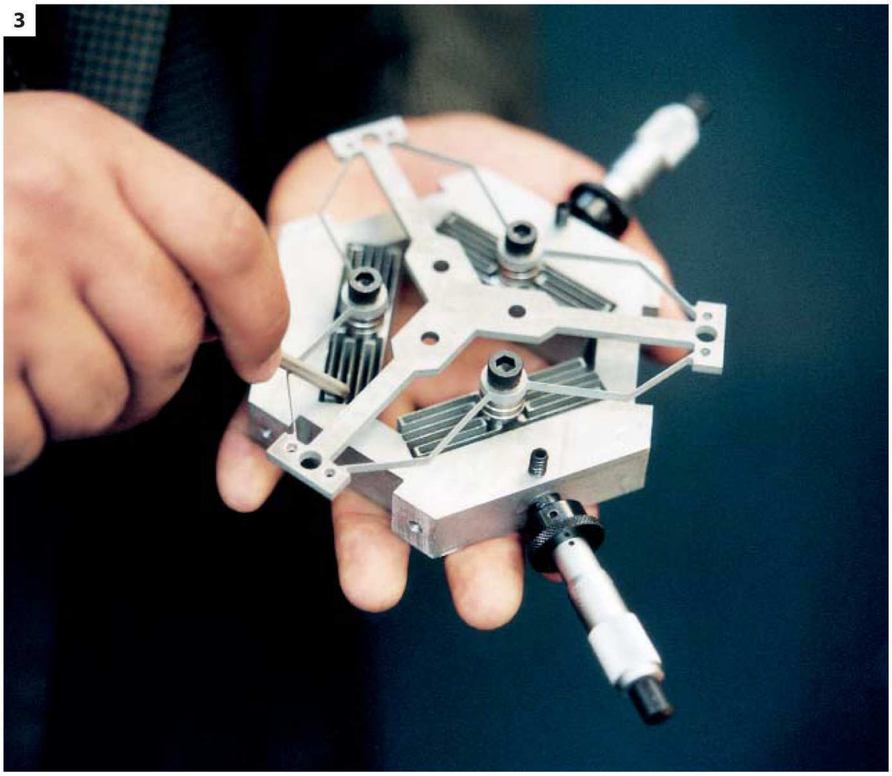

Culpepper can adjust the triangle's shape, tuning it to different tasks. "We can make it have a larger or smaller range of motion, or finer resolution," he explains, so that "people won't have to spend several thousand dollars just to do one task."

4–5. PRIME MOVERS. Culpepper next attaches the base to three actuators, the components that push and pull the flexible tabs on command. Each actuator consists of aluminum cylinders wrapped in hand-wound copper wire. Inside are long rod-shaped pieces capped on the ends with strong magnets. When current is passed through the wires, it creates a magnetic field within the actuator, pushing the magnets and mechanism to one side or another, or up and down.

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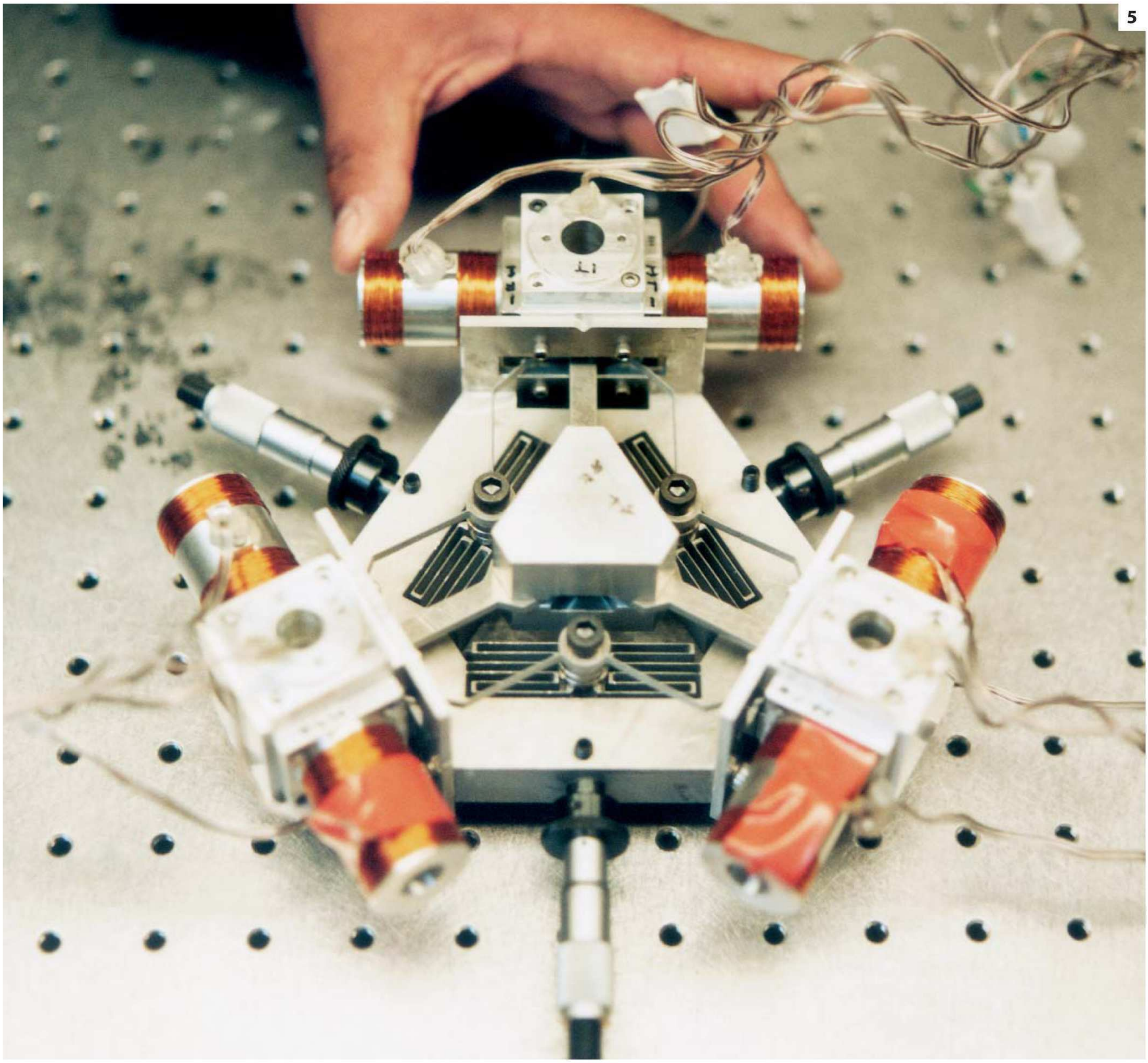
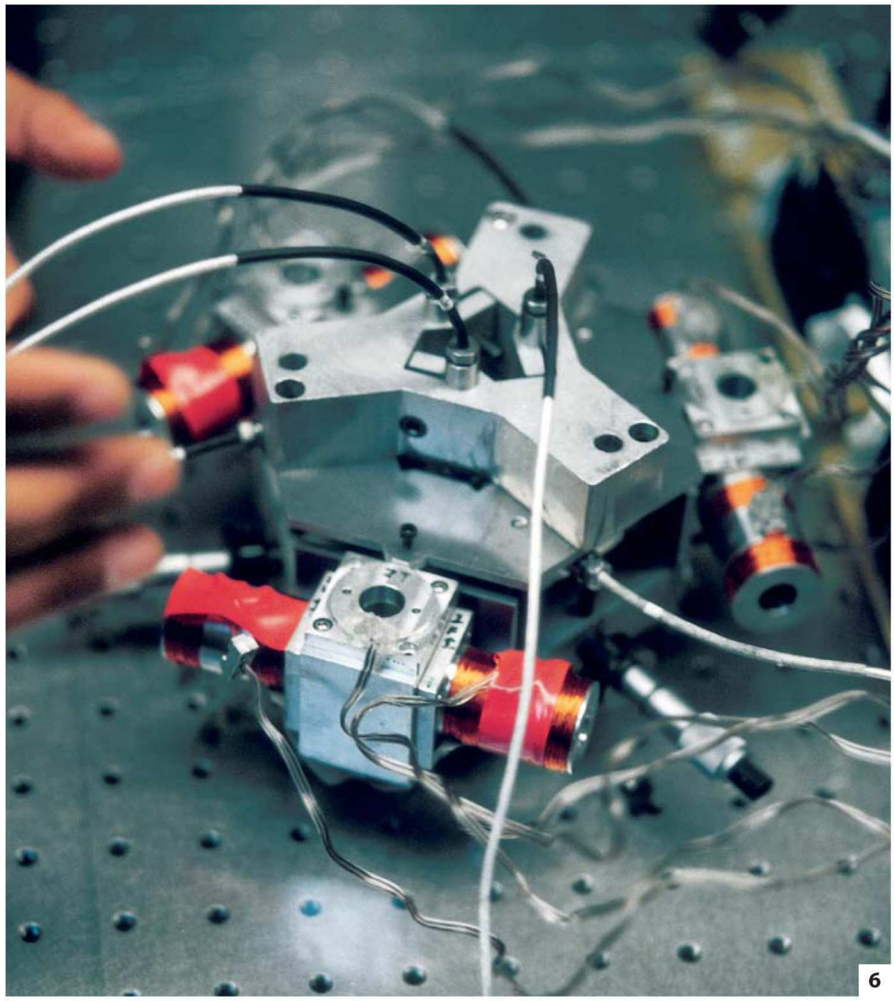


6. MIND THE GAP. On top of the device, Culpepper fixes a bulky piece strewn with wires. This tricornered aluminum crown contains six cylindrical capacitance sensors that precisely monitor the movement of the stage. Culpepper is contemplating a more compact, laser-based measurement system for future versions. "It can move without the sensors," he adds, "but at the levels of precision we're aiming for, it's critical to measure."

7. SILENT RUNNING. With the nanomanipulator assembled and wired up, Culpepper steps over to the computer to test it. It's not much for the naked eye to see, but as he types commands into the keyboard, the stage of the manipulator performs a nanoscale contortion routine. Culpepper keeps an eye on the numbers, watching for unexpected disturbances. Air vibrations stirred by ordinary voice conversations can throw the stage's position off, though careful structural design has minimized this effect. Lab instruments that incorporate the manipulator—which Culpepper will begin designing this fall—will be fully protected from these tremors. Coupon-clipping nanotechnologists may soon have cause to celebrate. TR



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Four-in-One Radio

BY CORIE LOK

ALL OVER THE WORLD, AND most recently in the United States, cellular companies have been upgrading their networks, moving from so-called second-generation, or 2G, technology to 3G systems that can deliver vastly more data at faster rates. Throw in the growing number of Wi-Fi connections, and mobile phones, PDAs, and other devices must contend with a tangle of networks speaking different languages at different frequencies. Since most wireless devices can handle only one of these languages and are permanently tuned to particular frequency ranges, they're unable to communicate outside limited geographic areas.

But a University of Waterloo, Ontario, startup called Sirific Wireless is developing a new chip that will enable wireless devices to use four wireless standards and tune to different frequency ranges. Such devices would be able to hop between networks looking for the fastest available data connections, regardless of location.

At the heart of any wireless device is the transceiver, which converts a radio signal to an electronic one and vice versa. Device makers have recently begun making mobile phones and PDAs that work on two different types of networks by equipping them with separate transceivers for each, an approach that adds bulk and cost. Sirific's newly designed transceiver can handle signals from the most common 2G cellular networks, enhanced second-generation networks dubbed 2.5G, 3G systems now being deployed around the world, and Wi-Fi, all on one chip.

SIRIFIC WIRELESS

HEADQUARTERS:
Santa Rosa, CA

UNIVERSITY:
University of Waterloo, Ontario

INVESTMENT RAISED:
$36.5 million

LEAD INVESTORS:
TD Capital, BDC Capital, Celtic House Venture Partners

KEY FOUNDER:
Tajinder Manku

What's more, the chip can be made using the industry-standard manufacturing process called CMOS (for complementary metal oxide semiconductor). "Anything you can get in CMOS you can make better, cheaper, more efficient at a much faster innovation rate," says Michael Hogan, Sirific's president and CEO. Most transceiver chips in today's cell phones are made using more-expensive specialty manufacturing techniques; Sirific estimates that the switch to CMOS could lower chip production costs by 30 percent.

This spring, Sirific raised $17 million in its third round of venture financing. The four-year-old company, which is based on research that founder Tajinder Manku began in 1996 as an electrical- and computer engineering professor at the University of Waterloo, has built a prototype wireless data card that includes its chip and other important radio components and has demonstrated it for several potential customers. One customer is building Sirific's technology into its product, a wireless module that would go inside laptops and PDAs. Hogan expects that, if all goes well, this product will hit the market by the first half of next year.

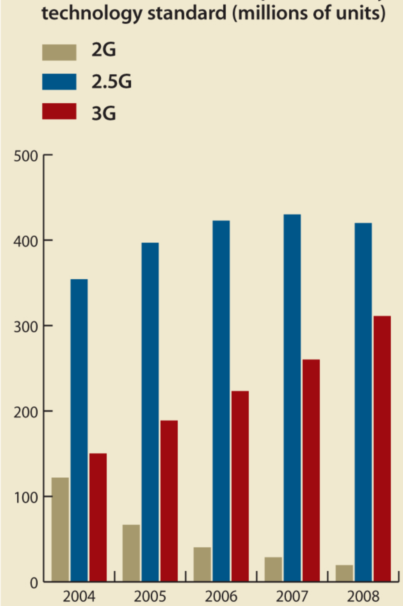
But the real prize for the company would be the nearly $3.5 billion global market for mobile-phone transceivers. Hogan hopes to have a chip ready for that market by early 2006.

Sirific will face plenty of competition, since most of the major radio chip makers, such as Texas Instruments and Qualcomm, plan to develop similar multimode products, says Stan Bruederle, research vice president at Gartner Semiconductor Research.

Still, with more than half a billion mobile phones sold worldwide this year—a number that is projected to rise steadily over the coming years—Sirific has a huge and burgeoning market to cash in on. TR

MOBILE PHONES GALORE

Worldwide handset unit production by technology standard (millions of units)



DESIGNERS OF NEXT-GENERATION RADIO CHIPS

COMPANY	TECHNOLOGY
Infineon Technologies (Munich, Germany)	Single-chip CMOS transceiver for 2G/2.5G handsets; shipped to first customer in July
Berkäna Wireless (Campbell, CA)	Single-chip CMOS transceiver for 2G/2.5G handsets and wireless modems
Silicon Laboratories (Austin, TX)	Single-chip CMOS transceiver for 2G/2.5G handsets and wireless modems
Quorum Systems (San Diego, CA)	Single-chip transceiver for Wi-Fi and 2G/2.5G voice and data communications
Ashvattha Semiconductor (San Diego, CA)	CMOS transceiver chip for handsets that can handle 2G/2.5G, Bluetooth, and GPS

SOURCE: GARTNER DATAQUEST (PHONES GALORE)

iPod

SINCE APPLE'S DIGITAL MUSIC PLAYER hit the market in 2001, four million units have sold. Both the device and the software that lets users manage its content work with Macintosh and Windows computers. The iPod connects to the computer via a cable or a dock that gives it access to the user's iTunes library and Apple's iTunes Music Store website. The site, launched in April 2003, has made legally downloadable music files a viable business, selling more than 100 million tracks. About ten thousand tracks fit on a 40-gigabyte iPod. Here's how it works. **TEXT AND ART BY 5W INFOGRAPHIC**

PLAYTIME

1. The user places the iPod in the dock, which connects to a Macintosh or Windows computer. With the iTunes software, the user can then load the iPod with digitally compressed music files—such as MP3s or Advanced Audio Code (AAC) tracks, which take up less space—from his or her iTunes library or from the iTunes Music Store website.

2. The device stores the songs on its hard drive and organizes them by album, artist, genre, and so on. The four-gigabyte iPod Mini can hold about 1,000 songs, while a 40-gigabyte iPod can hold about 10,000 songs in the AAC format.

3. When the user selects a song and presses "play," the iPod copies the digital music file from the hard drive to a memory chip*.

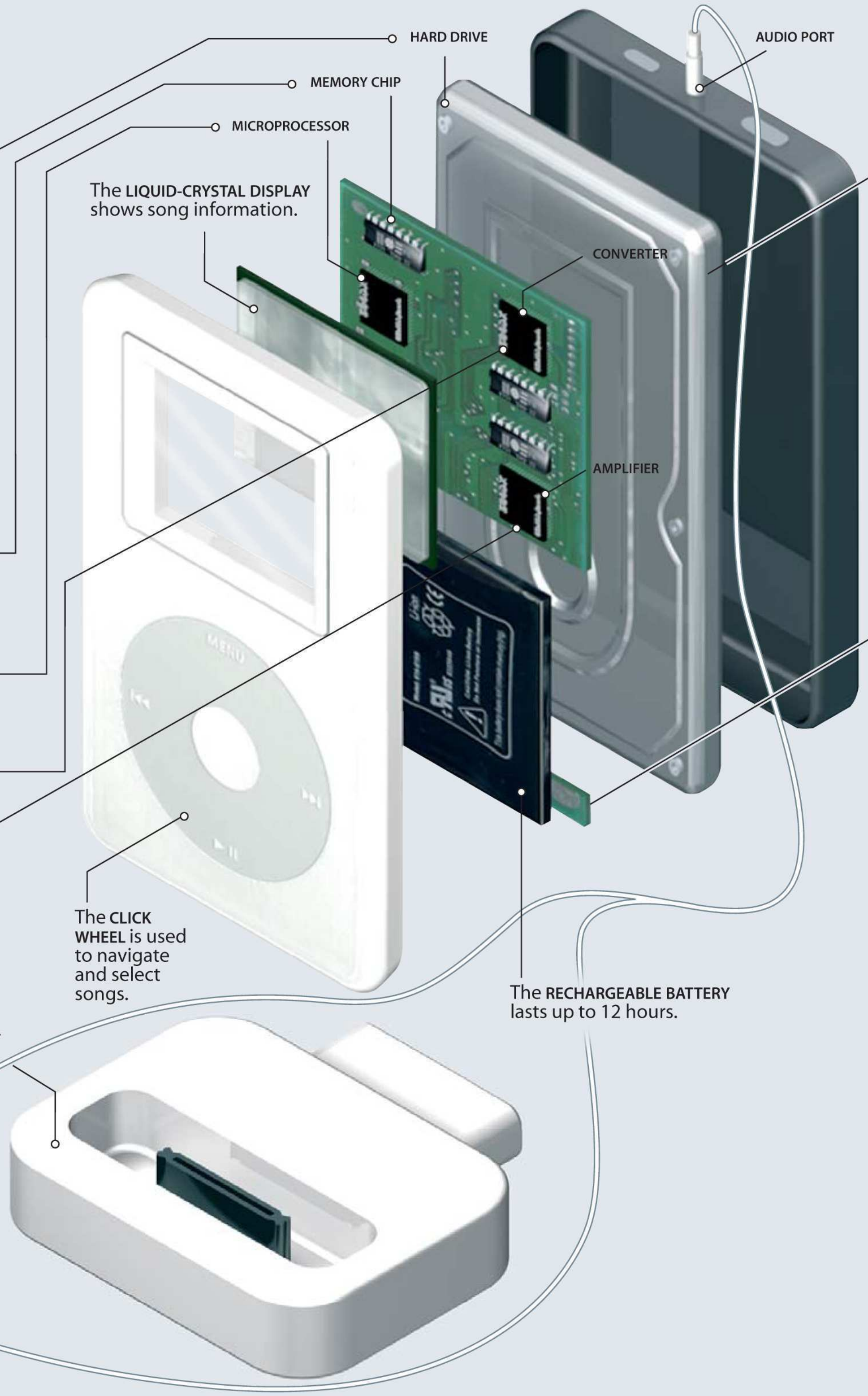
4. A microprocessor pulls the song from the memory chip and decompresses it.

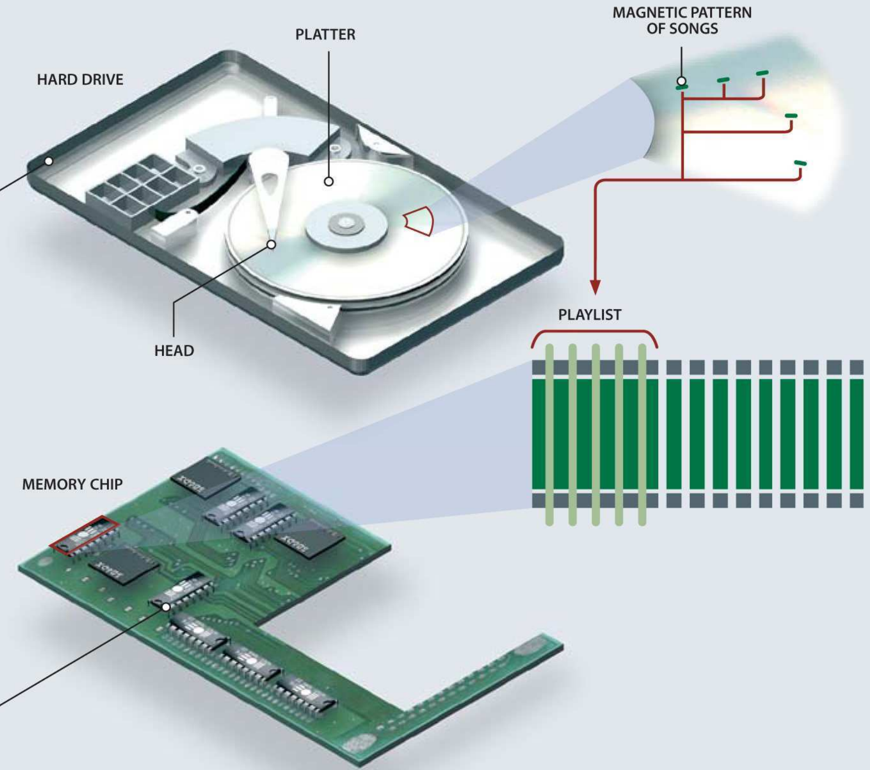
5. A digital-to-analog converter turns the digital data into an analog signal.

6. An amplifier increases the strength of the signal and sends it to an audio port, which can serve as a headphone jack.

*CIRCUIT BOARD ARRANGEMENT MAY VARY

The **DOCK** lets a user transfer and organize songs and recharge the iPod's battery.





SKIPPING OUT

If the iPod played music from its hard drive, the user's movements could jolt the components and cause a song to skip. So the iPod plays music from its memory chip, instead.

The iPod stores downloaded music files as magnetic patterns on a spinning platter. During playback, the device copies a "playlist"—about 32 megabytes, or 25 minutes, of music—from the hard drive to the memory chip. The hard drive then turns off until all of the music has played. The memory chip has no moving parts, so music files travel from it to the other electronic components without delay or error, even while a user is in motion.

MUSIC MANAGER

With the iPod connected to a computer, a user can easily change a playlist or purchase songs over the Internet.

Internet music stores

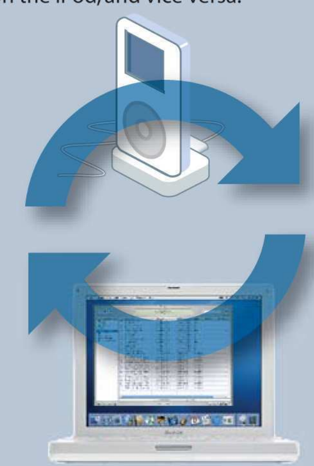
Simply by launching the iTunes music software, users with Internet connections can access the iTunes Music Store website, which is listed as a menu item. It offers approximately one million songs that cost about a dollar each; most albums cost $10 each. Users may burn downloads onto an unlimited number of CDs and transfer them to an unlimited number of iPods, and they can play downloads on up to five computers.

To and from CDs

In one fell swoop, the iTunes software can copy a track from a CD and compress it into MP3, AAC, or another format. Once the user adds the song to her library, she can transfer tracks to her iPod and create new playlists.

In sync

Every time the user connects the iPod to her computer, the iTunes software opens automatically. Playlist changes made on the iPod are updated on the iPod, and vice versa.



Option Play

HIDDEN UNDER A MENU NAMED "PREFERENCES" OR "Tools/Options," you will find a funny little control panel that contains a piece of software's heart and soul. ■ A common justification for preference panels is that there needs to be a way to customize programs, because each of us has different needs. An alternative explanation is that preference panels are a mark of neglect: unable (or unwilling) to figure out the "right" way to do something, the development team has thrown up its hands and dumped the decision on the user.

Both views have merit. Microsoft Word sensibly allows you to control whether to display formatting marks for tab characters, spaces, and end-of-paragraph marks. If you're writing letters to Aunt Jane, you probably don't want to see all of this visual clutter. But if you're editing a book or a magazine article, this kind of visual cue can be essential. On the other hand, Word developers abdicated their responsibility in the "Compatibility" panel, which allows control over such minutiae as whether SBCS characters should balance DBCS characters. I don't even know what these settings mean (apparently they relate to making documents compatible with previous versions of Word), but the developers did, and they should have picked the correct settings to ensure compatibility.

When I get a new program, one of the first things I do is systematically go through all of the options to see what the program is capable of. That's how I learned that Word has the ability to protect files so that they can't be read by someone who doesn't know the password ("Options/Security"). I discovered that Microsoft Outlook Express has an option to automatically spell-check my e-mail messages before sending them ("Options/Spelling"). And it turns out that my HyperSnap-DX screen capture utility can automatically scroll a window when taking a screen shot ("Capture/Capture Settings/Auto-scroll window"), which is great for capturing shots of really long Web pages.

Unable (or unwilling) to figure out the "right" way to do something, the development team has thrown up its hands and dumped the decision on the user.

Sometimes preference panels hide where you don't expect them. Find these panels: learning their powers will increase the number of things you can do with your software. For example, many programs can save documents in a variety of file types, such as text or rich text—two formats that can almost always be imported into other programs. You can usually find these types by choosing the "Save As…" menu option and then clicking on the "File Type" pull-down menu. But if you want to tell your Hewlett-Packard ink-jet printer that you're using photo paper instead of plain, you'll need to first open up the "Print" panel, then click on a button that says "Properties," and then select the "Paper" tab. Explore the other tabs and you will find a way to enable two-sided printing, print several page images on a single side of paper, or even print a watermark that reads "for internal use only" across every page.

Like strata in a city or scars on a soldier's back, preference panels frequently document past battles—either between the programmers and the project managers who created an application or between the company and its competitors. Microsoft Word versions for DOS displayed white text on a blue background; Word 2003 has an option to revert back to this prehistoric display, even though the color combination doesn't work well with today's fonts. Sadly, even companies that claim to care about usability keep loading more options into preference panels with each successive release of their software. For example, version 4.6 of Apple's iTunes program has seven(!) tabs on its preference panel, including one labeled "Advanced" that leads to a confounding assortment of additional choices.

Even my Palm handheld has a confusingly large number of preference panels: there's a set of systemwide settings in the "Prefs" application, more preferences on the Palm Desktop, and typically one or two additional preferences per application. Finally, there's an array of "conduit settings."

One of the things that mark me as an übergeek power user is my willingness to systematically identify and explore all of these various configuration screens and controls. I like to think of myself as a highly skilled programmer, but what makes me useful to my friends is my willingness to customize their systems by checking off the right boxes in the preference panels. It's not exactly virtuoso coding, but it's a skill that is becoming increasingly valuable.

That's because preference panels are standard fare now, not just on computer software but on printers, fax machines, cell phones, video cameras, and in-car navigation systems. My friend recently bought an electric range and was amused to find a preference panel that let him switch the language between English, Spanish, and French—and the temperature display from Fahrenheit to Celsius.

In the long run, true usability will come when we learn how to write software that needs less configuration, not more. TR

Simson Garfinkel is an incurable gadgeteer, an entrepreneur, and the author of 12 books on information technology and its impact.

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People and organizations mentioned in this issue

Charles F. Kettering (left) demonstrates his first self-starter to GM executives 25 years after its debut.

A Good Start

Charles Kettering's electric starter got rid of a major hassle for early drivers. **BY DAN CHO**

Assembly line production made cars cheap enough for the masses in the early 1900s, but it took a separate set of innovations to convince people to ditch their horse-drawn carriages for internal-combustion vehicles. One important innovation allowed motorists to start their engines without standing outside and turning metal cranks protruding from the fronts of their cars.

Crank starting was not only an inconvenient and laborious task but one that occasionally had nasty consequences. An engine misfire could cause the metal arm to jerk violently, sometimes causing sprains and broken bones. Henry Leland, president of Cadillac, knew firsthand the dangers; a friend of his was struck in the face by a wayward crank and died in the hospital from complications related to a broken jaw. The accident convinced Leland to pursue inventor Charles Kettering's proposal for an electric starter in 1910.

Kettering began his career in 1904 at National Cash Register in Dayton, OH, where he developed, among other things, an electric cash register that did away with the hand crank for cashiers. He left the company five years later to form his own inventing firm. It was during this time that he figured out a method for electric starting. The basic idea had been kicked around for more than a decade, but most engineers had concluded that a motor and battery powerful enough to spin the crankshaft would have to be nearly as large as the engine they were meant to start. Kettering, however, recalled a crucial insight from his NCR days: the motor needed to provide only a brief burst of power, turning just long enough to ring up a sale, or in this case, to turn over the engine. The hardware could be small because it would not be operating continuously.

Kettering and his assistants went to work designing their starter mechanism in the fall of 1910. By Christmas, they were testing a starter motor about a cubic foot in size. Cadillac soon agreed to include electric starters in its 1912 model. By 1920, when Kettering sold his research operation to Cadillac's parent General Motors, nearly every new car featured an electric-starter option. Kettering went on to direct GM's research for 27 years. TR

BETTMANN/CORBIS

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